LIMB SALVAGE PROCEDURES IN DIABETIC FOOT ULCERS - A PROSPECTIVE ANALYTICAL STUDY

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CERTIFICATE

This is to certify that this dissertation titled **"LIMB SALVAGE PROCEDURES IN DIABETIC FOOT ULCERS - A PROSPECTIVE ANALYTICAL STUDY "** submitted by **DR.P.SANGAIA RAJA** to the faculty of General Surgery, The TamilNadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MS degree Branch I General Surgery, is a bonafide research work carried out by him under our direct supervision and guidance from August 2009 to August 2011.

Prof.Dr. M.GOBINATH, M.S., M.S.,
Professor and Head of the Department,
Department of General Surgery,
Madurai Medical College,
Madurai.

Prof. Dr.S.MEENAKSHI SUNDARAM,
Professor & Unit Chief,
Department of General Surgery,
Madurai Medical College,
Madurai.

DECLARATION

I**, DR.P.SANGAIA RAJA** solemnly declare that the dissertation titled **" LIMB SALVAGE PROCEDURES IN DIABETIC FOOT ULCERS - A PROSPECTIVE ANALYTICAL STUDY"** has been prepared by me. This is submitted to **The TamilNadu Dr. M.G.R. Medical University, Chennai,** in partial fulfillment of the regulations for the award of MS degree (Branch I) General Surgery.

Place: Madurai **DR.P.SANGAIA RAJA**

Date:

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CONTENTS

TITLE : Limb Salvage Procedures In Diabetic Foot Ulcers – A Prospective Analytical Study

AIM OF THE STUDY

To assess the usefulness of various screening procedures and limb salvaging interventions in diabetic foot ulcers and to bring out strategies for prevention of future foot problems.

PATIENTS AND METHODS

This study was conducted at Government Rajaji Hospital, Madurai from August 2009 to August 2011. It included 100 patients with diabetic foot ulcers. Sensory neuropathy,vasculopathy and infection were evaluated using clinical and noninvasive methods. In infected ulcers wound healing between retrograde venous perfusion and intravenous antibiotics were compared. In non infected ulcers, wound healing was compared between platelet derived growth factor and normal saline dressings.

DATA COLLECTED

Age , sex , duration of diabetes ,treatment taken, smoking, hypertension and other comorbidities, were noted. Presence of sensory neuropathy, vasculopathy and infection were recorded. The ulcer area was assessed on days 0,7,14,21,28 in all

the patients and were categorized as completely healed, improved , partially healed and worsened .

RESULTS AND ANALYSIS

Most of our patients had type 2 diabetes and the mean duration was more than 7 years . Sensory neuropathy and vasculopathy were present in 100% and 80% of our patients respectively .In platelet derived growth factor application, about 80% of the ulcers improved and the reduction in ulcer area was more than 40cm2 by 4 weeks .By retrograde venous perfusion ,80% of ulcers improved and the reduction in ulcer area was around 41cm2 .All the patients are screened for the presence high risk pressure points and special foot wears were prescribed .

CONCLUSION

By adequate control of blood sugar,proper screening, appropriate foot care ,and judicious use of modalities like platelet derived growth factor application and retrograde venous perfusion of antibiotics most of the diabetic limbs can be saved.

KEYWORDS: diabetic foot, platelet derived growth factor, retrograde venous perfusion, sensory neuropathy, vasculopathy.

INTRODUCTION

Diabetes mellitus virtually affects every organ system in the body and it can be well said that "Knowing diabetes, is like knowing the entire human body". The Ancient Greek physician Aretaeus of Cappadocia (81 -138AD) was the first to use the term diabetes. The word diabetes is perhaps derived from a Greek word signifying a siphon. In 1920, Frederick Banting , Charles Best and John James Macleod first isolated insulin from the pancreas and named it isletin.

The world is currently experiencing a pandemic of diabetes mellitus, particularly of type 2 or adult onset. The magnitude of the problem of diabetes is enormous. By 2030 there will be 366 million diabetics in the world which is mainly due to longer life expectancy and change in dietary habits. India will have the largest number of persons with diabetes. Majority of these patients will be in the age group of 35 to 45 years. Approximately 15% of these patients will develop foot problems. And 1% of these patients are likely to lose a limb due to some foot pathology or the other. However, the blessing in disguise is that the foot problems seen in indian diabetic patients are mainly neuropathic-infective and not ischemic – infective. The latter are extraordinarily more difficult to treat than neuropathic ulcers.

It is a sad fact that , as of today a regular foot examination and monitoring is not routinely practiced by our people. In fact, the routine policy is – "No complaints – No examination". However, by the time the patient complains of some symptoms, the pathology is advanced and foot salvage becomes extremely difficult. Early detection and attention to warning signals in the foot definitely can salvage the limbs to a greater extent.

DIABETIC FOOT

Definition

The diabetic foot may be defined as a group of syndromes in which neuropathy, ischemia, and infection lead to tissue break down resulting in morbidity and possible amputation".

WHO definition :

"The foot of a diabetic patient that has the potential risk of pathologic consequences including infection, ulceration and / or destruction of deep tissues associated with neurologic abnormalities, various degrees of peripheral vascular disease and or metabolic complications of diabetes in the lower limb".

Government Rajaji Hospital, Madurai.

This renowned institution which is well known for its academic and research activities has a very good infrastructure for managing diabetes and its associated complications. In our institution we have a diabetology department and also a diabetic foot clinic for effective management of foot problems in diabetes.

Department of Diabetology

This department has a well equipped infrastructure, which has been rendering its services to all the diabetics of southern districts of Tamilnadu from the year 2000 onwards . It is manned by fully qualified diabetologists who are treating about 800 to 1000 diabetic patients per day as outpatients. Various screening tools like biothesiometer, doppler probe and other sophisticated equipments are available in this department. Experts in the field of dietics and podiatry educate our diabetic patients to have a better quality of life.

Diabetic foot clinic

In the department of General surgery, we have a separate diabetic foot clinic in which we conduct separate outpatient clinics once a week. Every week we do get around 10- 15 diabetic patients with foot problems who will get

either an outpatient or inpatient treatment depending on the magnitude of their problem. In addition to this, patients with diabetic foot ulcers are being admitted in regular OPD's also. All these patients are treated according to current guidelines and recommendations. There is a separate physiotherapy department where proper foot wear is being dispensed for the diabetic patients with foot problems.

AIM OF THE STUDY

To assess the usefulness of various screening procedures and limb salvaging interventions in diabetic foot ulcers and to bring out strategies for prevention of future foot problems.

1. To evaluate the incidence of sensory neuropathy, vasculopathy, infection and its association to diabetic foot ulcers.
2. To compare the effectiveness of wound healing in diabetic foot ulcers

   a. Between application of Platelet derived growth factor and Saline dressings.

   b. Between Retrograde venous perfusion and Intravenous administration of antibiotics.

MATERIALS AND METHODS

This study was conducted at Government Rajaji Hospital, Madurai from August 2009 to August 2011. It included 100 patients with diabetic foot ulcers who got admitted in surgical wards. Patients treated as outpatients were excluded from the study .The diagnosis of diabetes was verified for all patients using the criteria set forth by the World Health Organization which includes, treatment with insulin, two random blood glucose measurements greater than 200mg/dl or a fasting blood glucose greater than 126mg/dl. Age and sex of the patients, duration of diabetes and treatment taken were recorded. Presence of smoking, hypertension and other comorbidities were also noted. Sensory neuropathy was evaluated using foot imprints with harris mat and biothesiometry. The areas of high pressure in the foot which is marked by the presence of more ink in the imprints and a vibration perception threshold of more than 25v in biothesiometry are taken as presence of sensory neuropathy.

A working diagnosis of lower extremity ischemia was made by a combination of clinical and noninvasive vascular studies. Clinical signs were based on the absence of one or more foot pulses of the involved foot. Noninvasive criteria included an Ankle – Brachial index (ABI) of < 0.80. Clinical signs and / or the presence of abnormal noninvasive values make a diagnosis of lower extremity vascular insufficiency.

The diagnosis of infection was made using clinical criteria. Wounds with frank purulence and / or two or more of the following local signs were classified as “infected”. These signs include warmth, erythema, lymphangitis, lymphadenopathy, edema, and loss of function. Culture and sensitivity of the wound discharge was also done. Effective wound debridement was done in all the cases. And all the patients were treated with insulin.

In infected cases the role of retrograde venous perfusion of antibiotic was compared with intravenous antibiotic with respect to the decrease in ulcer area on days 0, 7, 14, 21, 28. Before the institution of retrograde venous perfusion assessment of vascular status of the limb was done by doppler study. Combination of Heparin(100units), Sodium bicarbonate(2ml), Piperacillin +Tazobactum(4.5g) and Lignocaine (4ml) made to 120ml with normal saline was injected in to leg vein with application of tourniquet at the thigh for 20 minutes. Intravenous piperacillin+tazobactum alone was given in the intravenous group. Antibiotics were given for a period of 14 days in both the groups. The inclusion criteria were (a) patients with infected non healing diabetic foot ulcer (b) absence of venous thrombosis in the affected limb and (c) nonedematous limbs. The exclusion criteria were, presence of deep vein thrombosis, gangrene and difficulty in venous canulation.

In non infected diabetic foot ulcers the effectiveness of wound healing was compared between the application of platelet derived growth factor and saline dressings. Daily application of platelet derived growth factor was done for a period of one month and normal saline dressing in the control group and the ulcer area was assessed on days 0,7,14,21,28 in both the groups.

Ulcer Healing in all the groups were categorized as **A**-Completely healed, **B**-Improved (>80% reduction in ulcer area), **C**-Partially healed (<50% reduction in ulcer area) and **D**-Worsened . Other treatment modalities like skin grafting and amputation were also recorded.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EIP 2010)** developed by Centre for Disease Control, Atlanta. Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

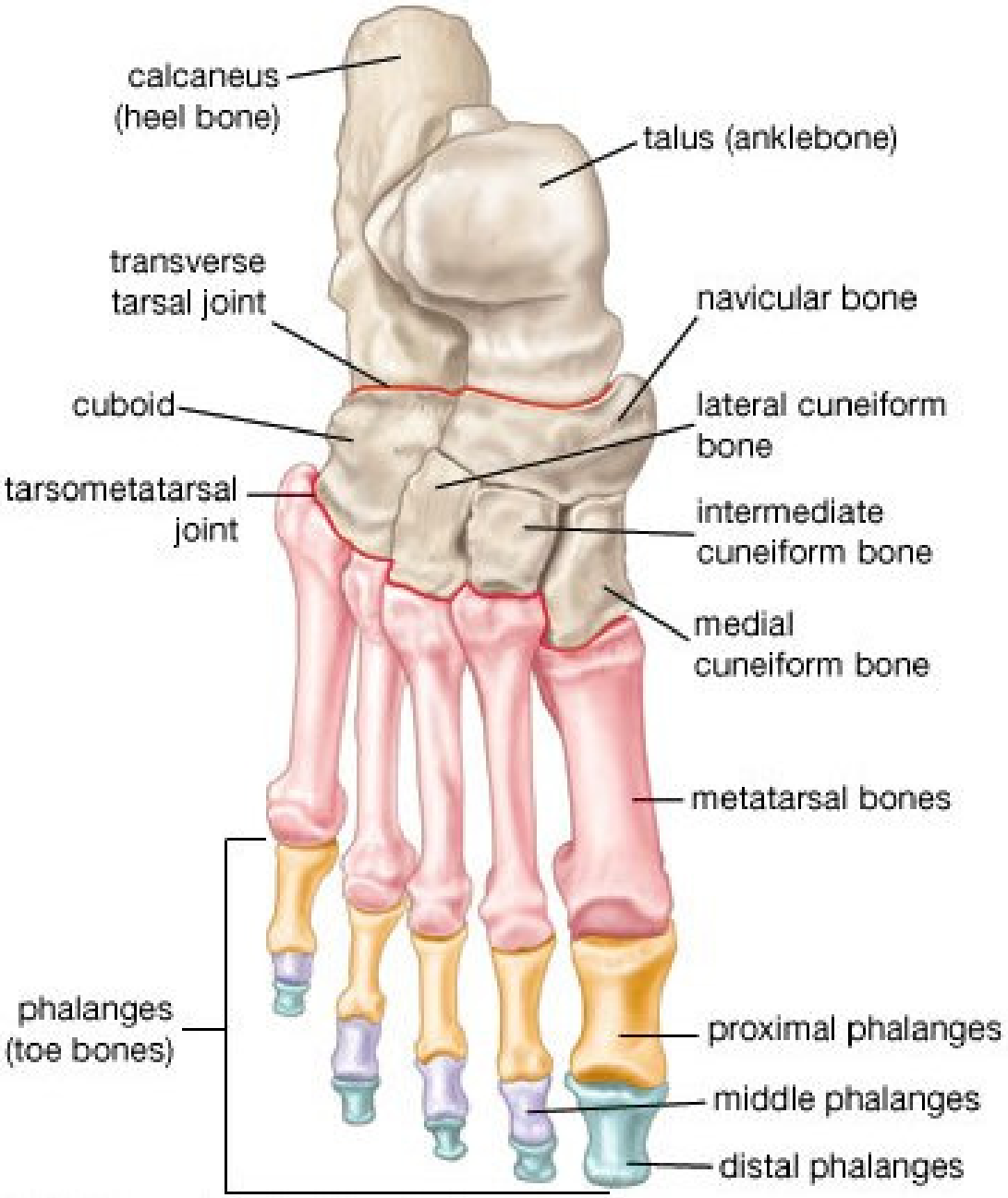
DIABETIC FOOT – MORBID ANATOMY

A sound knowledge of anatomy is essential while treating diabetic foot complications, particularly infections. Unless aggressively and adequately treated for infections, “the patient pays through his foot’ and may ultimately go home without it”.

Peculiarities of the foot

“Foot is a highly complex design of nature, energy efficient, shock proof and has resilient biomechanism, adopted to weight bearing and locomotion on uneven surfaces”. The foot is more peculiar so that it a vulnerable target in diabetes. It is the farther point from the heart and hence the commonest site for arterial insufficiency. It is the most dependent part of the body there by a favorite site for venous insufficiency. It is the maximum weight bearing part and hence there are multiple pressure points which are poor prospects for survival of free skin grafts. The foot is vulnerable to injuries. It is also a common site for peripheral neuropathy, wherein the foot is vulnerable to physical and thermal injuries, small muscle atrophy and deformities as well as trophic changes. The foot is also prone to footwear related problems like blisters (new shoes), corn or callosities, ingrown toe nail, hallux valgus and

SKELETON OF FOOT



hammer toe. Due to socio cultural practices, there are problems related to bare foot walking.

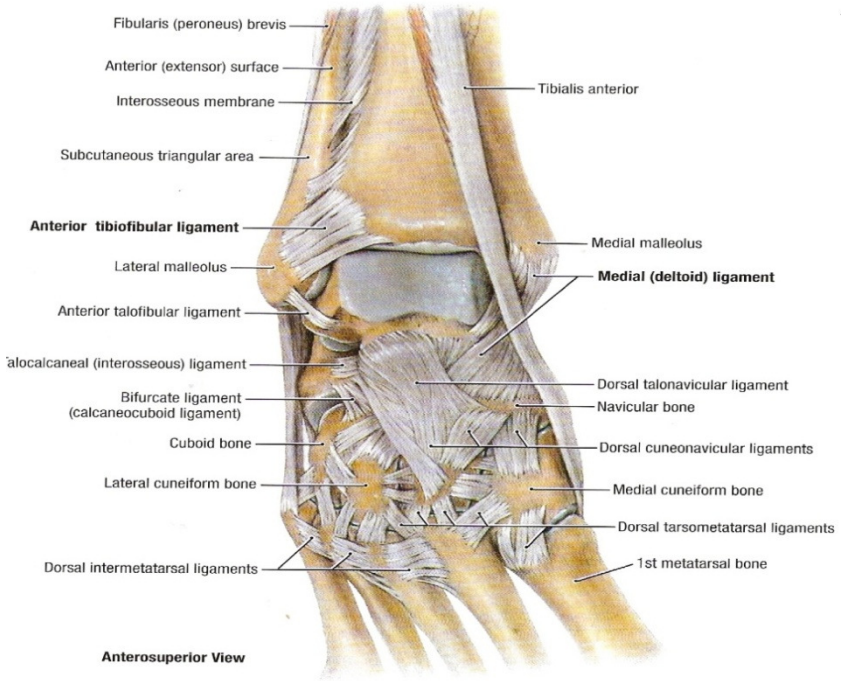
Skin , Nails and Subcutaneous tissues of the foot

The dorsal skin is thinner (2mm thick), lax and can be pinched, while the plantar skin is thick (5mm) and cannot be pinched. The foot has a thick stratum corneum and a thin dermis. The skin is rich in sweat glands on the plantar skin. The dermis is bound to underlying fascia to improve grip and to prevent gliding or sliding. Infections of sole tend to point to the dorsum, because of the thick plantar skin. The epidermis gets transformed into the nail matrix. It has three ill- defined layers dorsal, intermediate and ventral layers. It is firmly attached to the epithelium of nail bed. The margins of the nail are overhung by skin folds predisposing to ingrown toe nails.The plantar subcutaneous tissue is more fibrous. The fluid fat is loculated by fibrous septa to provide shock absorption and to prevent gliding or sliding of plantar skin.

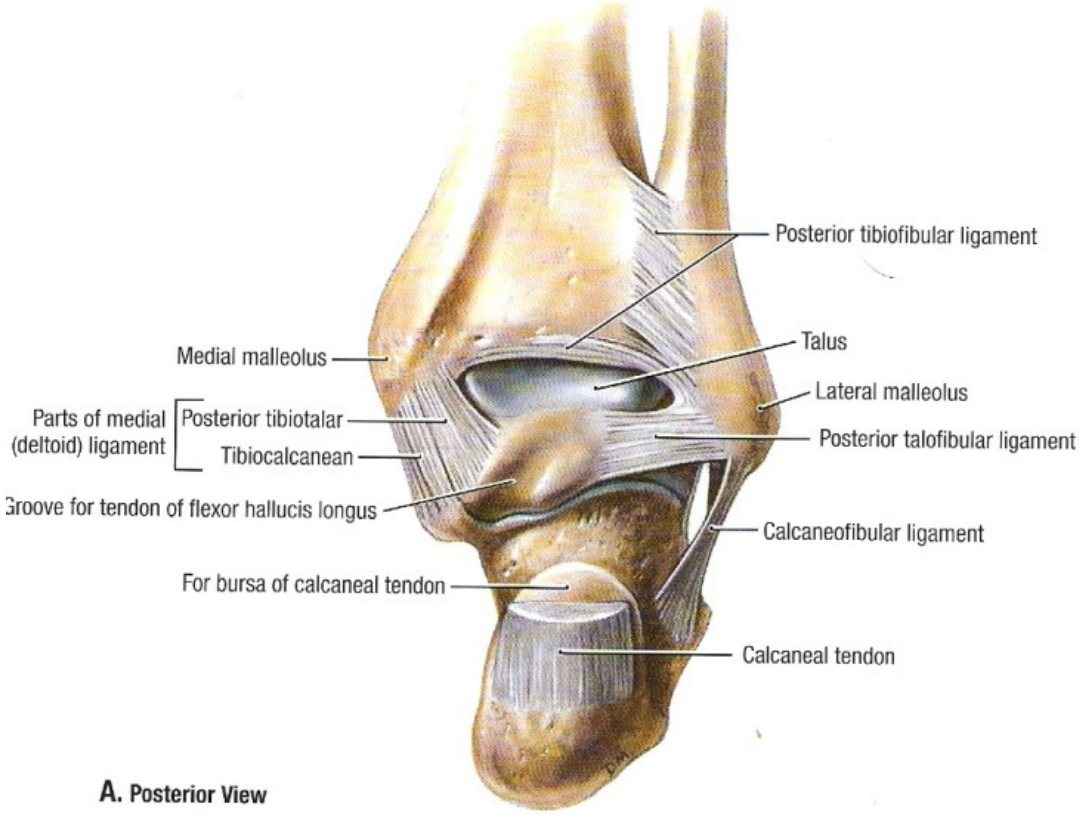
Skeleton and fascia of the foot

The skeleton of the foot is shaped to form arches and adjust to uneven surfaces. There are 7 tarsal bones, 5 metatarsals and 14 phalanges.The superficial fascia of the sole is fibrous and dense. Fibrous bands bind the skin to deep fascia or plantar aponeurosis. The fibrous bands divide the

LIGAMENTS OF FOOT



Anterosuperior View



A. Posterior View

subcutaneous fat into small compartments which serve as cushions and reinforce the spring effect of the arch during walking, running, jumping, etc.

The fascia is thick over weight bearing parts. It contains cutaneous nerves and vessels. The thickened central part of the deep fascia is the plantar aponeurosis. The plantar aponeurosis fixes the skin of the sole, protects deeper structures and helps in maintaining the longitudinal arches of the foot. It also gives origin to the muscles of the first layer of the sole.

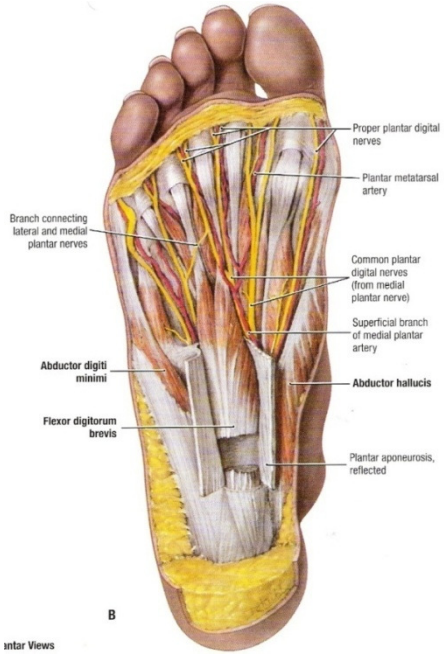
Ligaments of the foot

The ligaments maintain the arches and stability. They have a springing effect in locomotion and also help in shock absorption. The ligaments of the foot are long plantar ligament, plantar calcaneocuboid (shortplantar) ligament, plantarcalcaneonavicular (spring) ligament, deltoidligament (medial), transverse metatarsal ligament, interosseous ligament.

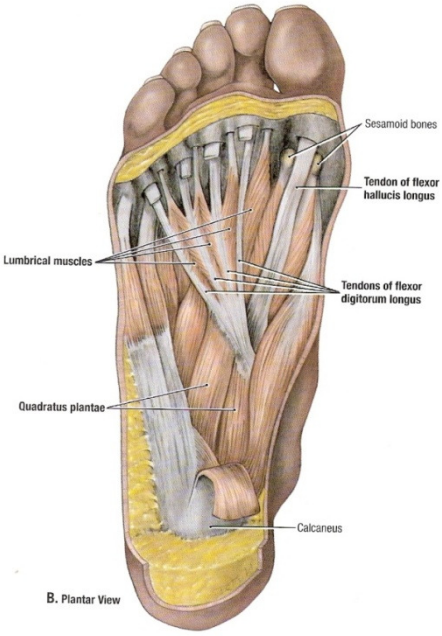
Muscles and tendons of the foot

There are four layers which help in movement and grip and have a cushioning effect thereby protect nerves and vessels and they suspend arches. First layer includes abductor hallucis longus, flexor digitorum brevis, abductor digiti minimi. Second layer is made of flexor accessorium (quadratus plantaris), tendons of flexor hallucis longus, flexor digitorum longus and the

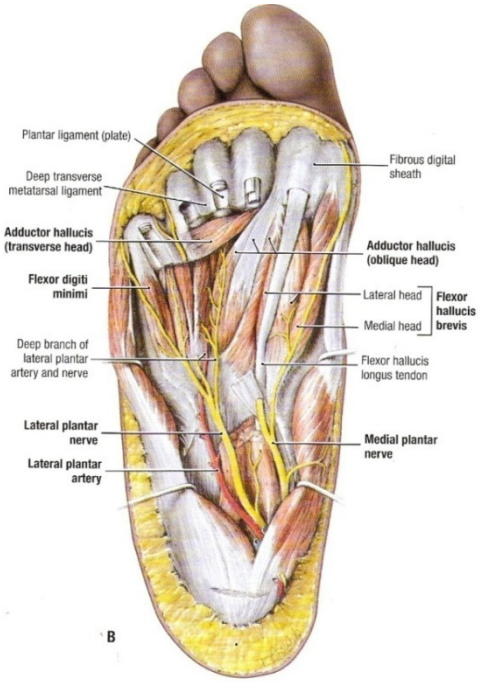
SOLE OF FOOT



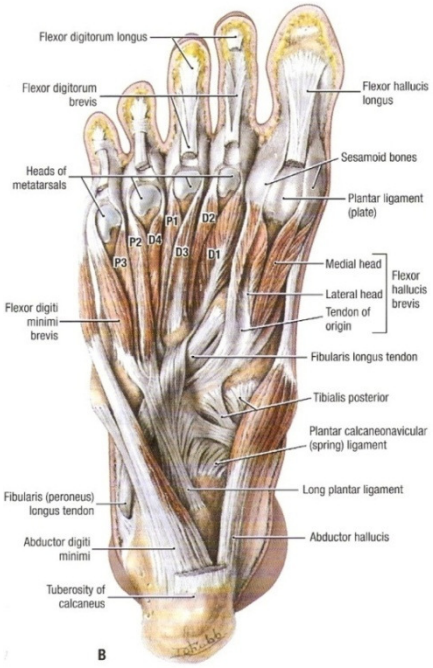
First layer



Second layer



Third layer



Fourth layer

lumbricals. Third layer is constituted by the flexor hallucis brevis, , transverse and oblique heads of adductor hallucis, flexor digiti minimi brevis. The fourth layer is mainly formed by the interrossei.

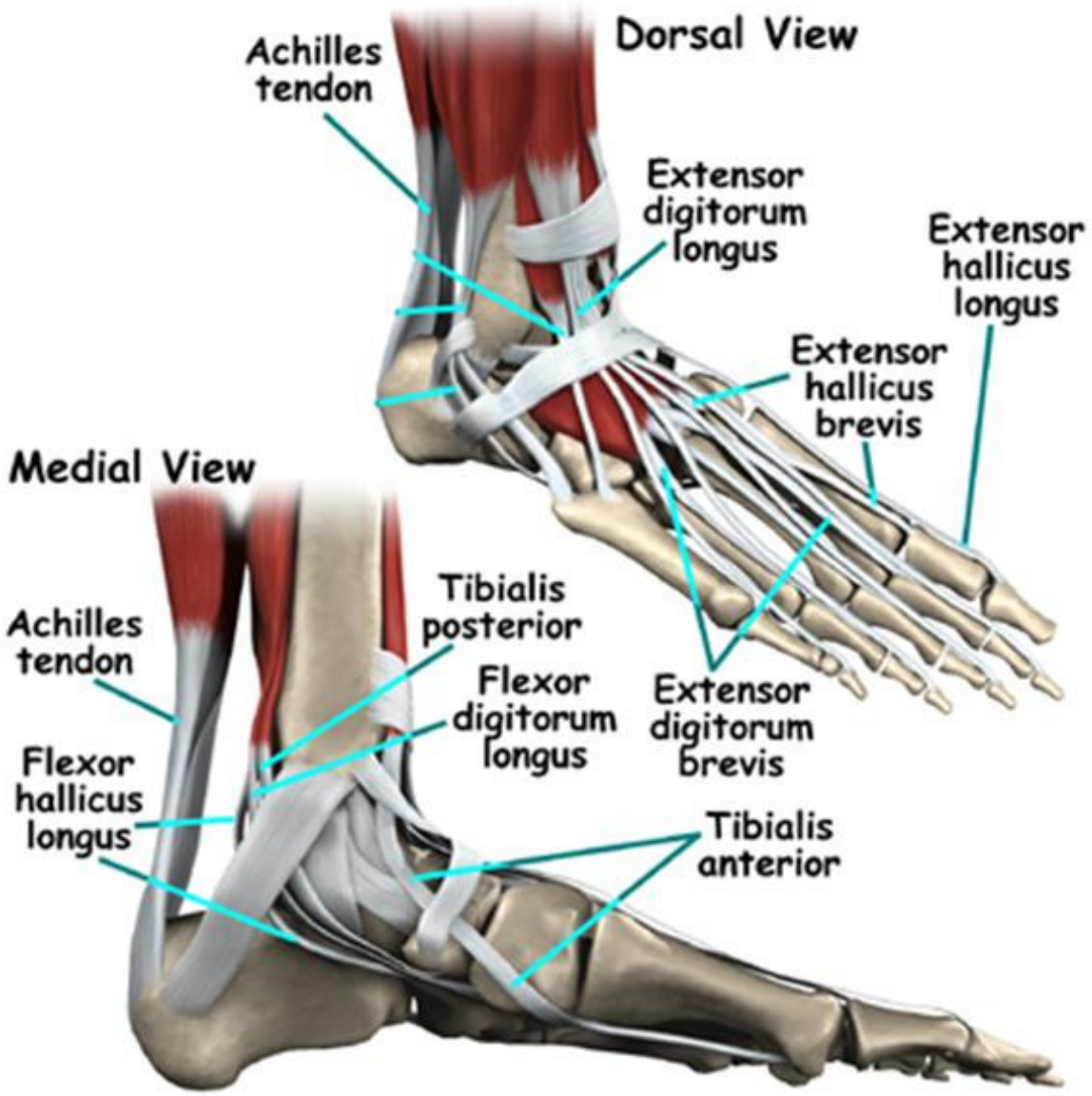
Musculo- fascial compartments of the foot

There are four compartments, formed by vertical septa from the plantar aponeurosis extending deep. They are the medial, central, lateral and interosseous compartments. The medial compartment contains medial plantar nerve, artery, vein, and the central (larger) compartment contains lateral plantar nerve, artery and vein.

Nerves of the foot

Saphenous nerve arises from the femoral nerve. It supplies medial aspect of the foot up to the first metatarsal. **Superficial peroneal (fibular) nerve** is the smaller terminal branch of the common peroneal nerve. It gives cutaneous branches to most of the dorsum of foot including digital branches to medial side of great toe, adjacent sides of second, third, fourth and fifth toes. **Deep peroneal (fibular) nerve** is the terminal branch of the common peroneal nerve. It supplies extensor digitorum brevis and gives cutaneous branch to the adjacent side of great and second toes. **Medial plantar nerve** is the largest terminal branch of the tibial nerve. It supplies abductor hallucis, flexor

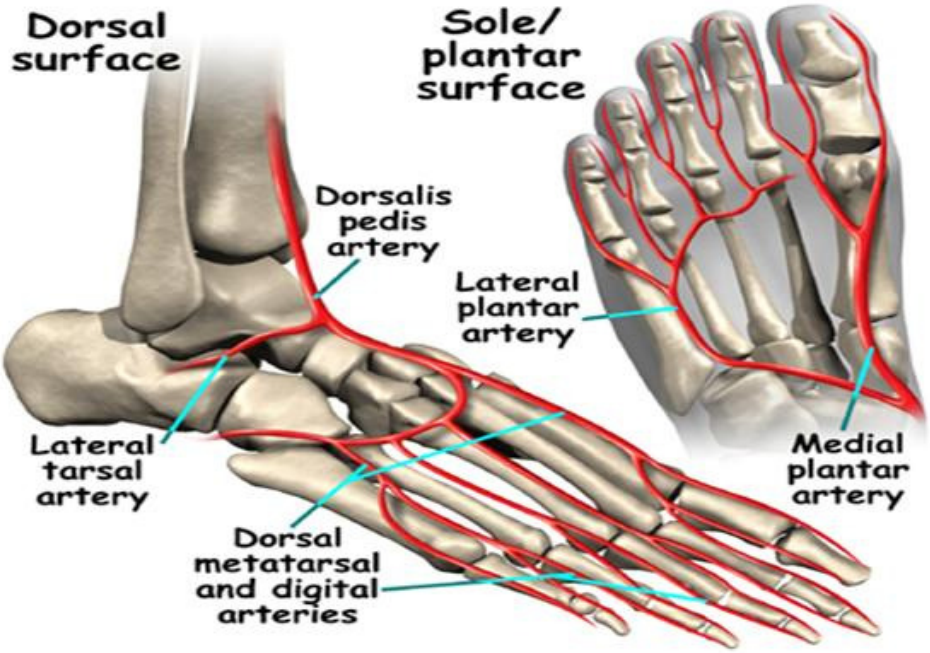
TENDONS OF FOOT



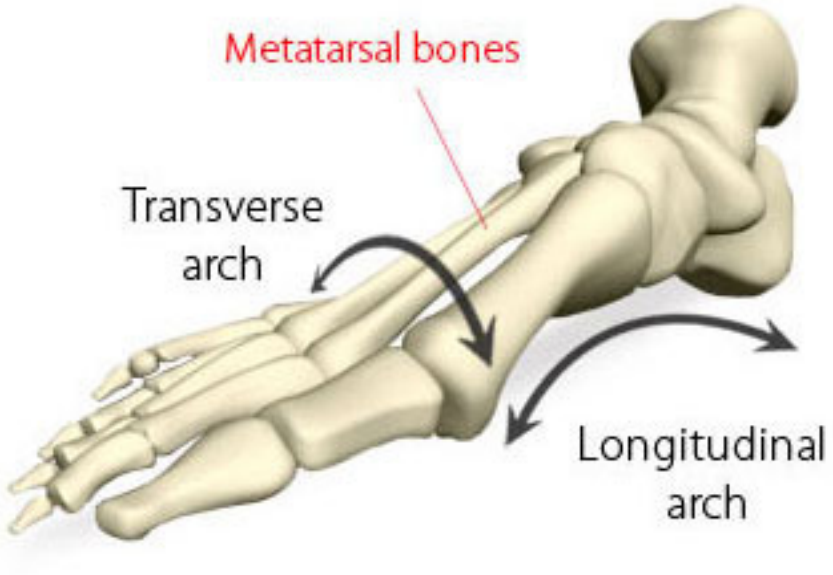
digitorum brevis, flexor hallucis brevis and first lumbrical muscle. Cutaneous branches supply skin of the medial part of the sole and medial three and half toes. **Lateral plantar nerve** is the smaller terminal branch of tibial nerve. The main trunk supplies flexor digitorum accessorius, abductor digiti minimi and skin of the sole. It divides into superficial and deep branches. **Sural nerve** arises from tibial and common fibular nerves and runs along the short saphenous vein. It supplies lateral side of the foot and fifth toe and all intrinsic muscles of the foot (S2 and S3).

Arterial tree

The dorsalis pedis artery is a continuation of anterior tibial artery and it runs between tibialis anterior and extensor hallucis longus tendons. It may be absent in about 5% of population. It gives arcuate artery, supplying the dorsum of foot and toes. The dorsalis pedis artery dips deep in the first inter-metatarsal space to form the plantar arch, by joining the medial and lateral plantar arteries. The posterior tibial artery, runs behind the medial malleolus and divides into medial and lateral plantar arteries, supplying the sole and toes. The plantar arch is formed by the medial and lateral plantar arteries with contribution from termination of the dorsalis pedis artery. The digital arteries arise from the plantar arch (plantar aspect) and arcuate artery (dorsally).



VESSELS OF FOOT



ARCHES OF FOOT

Venous drainage

The dorsal venous arch lies in the dorsum of foot over the proximal parts of the metatarsal bones. It receives four dorsal metatarsal veins. These metatarsal veins are formed by the union of two dorsal digital veins.The long saphenous vein is formed by the union of medial end of the dorsal venous arch and the medial marginal vein. The medial marginal vein drains the medial side of the great toe. The short saphenous vein is formed by the union of lateral end of dorsal venous arch and lateral marginal vein. The lateral marginal vein drains the lateral side of the fifth toe. Both the saphenous veins connect to deep veins through the perforating veins.

Lymphatic drainage

Superficial lymphatics drains along both the saphenous veins, short saphenous zone into popliteal group and long saphenous zone into inguinal group. Deep lymphatics drain along the arteries to both popliteal and inguinal groups.

Arches of foot

The arches help to adjust to uneven surfaces. The presence of arches makes the sole concave and this concavity protects the neuro-vascular structures. They are medial and lateral longitudinal arches and the anterior and posterior transverse arches

Anatomical principles of surgical incisions

There are some anatomic principles one need to keep in mind while making incisions on the foot.

- Avoid neuro-vascular injury.
- Avoid weight- bearing points.
- Make liberal counter incisions.
- Deroofing should be liberal.
- Excise metatarsal head, while doing toe amputation for better realignment of toes.

DIABETIC FOOT - PATHOPHYSIOLOGY

Diabetes mellitus is associated with more than half of all non-traumatic lower limb amputations. The major pathophysiological factors are ischemia, neuropathy and wound infection. They operate concurrently and sequentially, enhancing the risk for amputation fifteen fold in diabetic subjects compared to non diabetics. Since the diabetic foot is the sequelae of interaction of multitude of factors, intervention must be directed towards correction of all causative factors.

Diabetic neuropathy

The most important factor leading to amputation for the person with diabetes is peripheral neuropathy and the resulting insensitive foot. Diabetic neuropathy affects sensory, autonomic and motor neurons of the peripheral nervous system, which is to say that every type of nerve fibre is affected. Diabetic peripheral neuropathy may be divided into two main types, acute sensory neuropathy and chronic sensorimotor neuropathy(most common).

Biochemical dysfunctions leading to neuropathy includes increased advanced glycosylation end products(AGE'S),defective polyol pathway, neuro vascular alterations and impaired resistance to oxidative stress. The manifestations of sensory neuropathy are paresthesia, reduced pain perception, loss of joint sense, loss of vibration sense, glove and stocking anaesthesia,

charcot joints. Motor neuropathy presents as weakness of muscles, paralysis of small muscles of foot producing deformed toes. Autonomic neuropathy is characterized by the micro circulatory derangement of the tissues of the foot. There will be abnormal sweating and in some absence of sweating, dry foot with lot of cracks in the sole, calcification of medium sized arteries and loss of thermoregulation.

Development of neuropathic ulcer

Increased load

↓

Unaware due to insensate foot

↓

Focused inflammation

↓

Plaque of keratin

↓

Tissue breakdown

↓

Cavity as nidus of sepsis

↓

Invasive infection

↓

Trophic ulcer

Diabetic Macroangiopathy

Involvement of the major blood vessels is common in diabetes. The abdominal aorta and its branches are affected. The atherosclerosis is 20 times more common in the diabetics than the non diabetics. Calcification of the artery is also a common feature of diabetes. The media of the artery is calcified, which is called as Monckeberg sclerosis and this is due to neuropathy.

Calcification makes the vessel rigid and this gives a falsely elevated perfusion pressure. The crucial artery is the popliteal artery and its narrowing produces foot gangrene. Diabetes and smoking are the strongest risk factors for peripheral arterial disease. It is important to note that diabetes is most strongly associated with femoral – popliteal and tibial (below the knee) peripheral arterial disease. Diabetic peripheral arterial disease has predilection for tibial and peroneal vessels but dorsalis pedis artery, the distal posterior tibial artery and the plantar arteries are usually spared. Diabetic patients with atherosclerotic peripheral vascular disease also show a diminished ability to establish collateral circulation.

Microvascular changes

Peculiar to diabetes is development of microvascular dysfunction, which begins early in diabetic life. It is frequently seen in the capillaries and arterioles of kidneys, retina and peripheral nerves, but spares no organ. In diabetes RBC's become flat and rigid and the blood is more viscous which are the major factors for microvascular impairment. Abnormalities in nitric oxide pathway, abnormal vasoconstrictor prostanoids, intracellular signaling , reduction in sodium- pottasium ATPase activity, and advanced glycosylation end products are responsible for microvascular changes.

Vascular diseases:

The frequently associated risk factors for diabetic vascular disease include smoking, hypertension, hyperlipidemia, insulin resistance with compensatory hyperinsulinemia, severity and duration of diabetes, age and genetic factors. Smoking enhances the risk of peripheral vascular disease more than hundred times compared to non – diabetic non smokers. However, cessation of smoking has been associated with a decrease in the progression of atherosclerosis.

Hypertension is twice as common in diabetics as compared to non diabetics; roughly one third to one half of diabetics have hypertension. Systolic hypertension has been linked with disease of proximal blood vessels.

Diabetes and endothelial cell dysfunction

The mediator of endothelial cell dysfunction in diabetes is derangement of nitric oxide bioavailability. Nitric oxide inhibits vascular smooth muscle cell migration and proliferation and limits platelet activation. Diabetes stimulates proatherogenic activity in vascular smooth muscle cells.

Diabetes, coagulation and rheology

Diabetes leads to hypercoagulable state. It is associated with the increased production of tissue factor by endothelial cells and vascular smooth muscle cells as well as increased plasma concentration of Factor VII.

Hyperglycemia is also associated with a decreased concentration of antithrombin and protein C, impaired fibrinolytic function, and excess production of plasminogen activator inhibitor. **Platelet** aggregation is enhanced in diabetes. Platelet in diabetic patients also have increased expression of Glycoprotein IIb/ IIIa receptors, which are important in thrombosis via their role in platelet adhesion and aggregation.

Infection

Infection is defined by invasion of the tissues with proliferation of microorganisms causing tissue damage with or without an associated

inflammatory response by the host. Foot sepsis accounts for about 70% of all infections. Adherence of granulocytes and other WBC functions like phagocytosis are impaired in diabetes. T cell function is impaired and cell mediated immunity is depressed. Hyperkeratosis in foot is mistaken for a corn and removing it using rusted nail and safety pin is the foremost reason leading to amputation. Absent sweating leads to cracks and fissures in foot which are portals of infection. Organisms may be causative , commensal, contaminant or coexisting polymicrobial. Most common is polymicrobial infection. Staphylococcus aureus and Beta hemolytic streptococci are the most commonly involved pathogens in acute infections. In Chronic wounds, Enterococci, Enterobacteriaceae, Obligate anaerobes, Pseudomonas, Fungi are the pathogens involved.

Biomechanical aspects:

Combination of neuropathy and trauma results in tissue breakdown. The atrophy of the intrinsic muscles of the foot, predominantly plantar flexors of the toes alters the flexor / extension balance at the metatarsophalangeal joints and causes clawing of the toes and prominence of the metatarsal heads. Alterations of foot shape results in increased plantar pressure. A majority of wounds on insensitive foot are not caused by accidental injury or ischemia but from continuous pressure. Often moderate stress as occurring during

CHARCOT FOOT

locomotion on the same part of the insensitive foot leads to callus formation and ulcer. The presence of callus may exacerbate the problem both acting as a foreign body and by increasing the plantar pressure.

CHARCOT FOOT:

Charcot foot or neuroarthropathy is defined as a relatively painless, progressive, degenerative arthropathy of single or multiple joints caused by underlying neuropathy. Charcot neuropathy is characterized by simultaneous presence of bone and joint destruction, fragmentation and remodelling. Diabetes is the commonest cause of charcot foot and most patients have a dense neuropathy but good circulation. Walking on an insensitive foot leads to excessive and repetitive stress to bone causing micro fracture and finally bone and joint destruction. Diabetic neuropathy and presence of auto sympathectomy lead to peripheral vasodilatation (warm foot). A significant arteriovenous shunting takes place leading to abnormal bone cell activity (osteoclastic) and eventual resorption and weakening of bone. Ultimately the foot shape is deformed and runs into a bag of bones.

Bone and joint damage in the metatarsal region is the commonest site of involvement and leads to the two classical deformities.

1. Rocker bottom deformities in which there is displacement and subluxation of the tarsus downward.
2. Medial convexity, which results from displacement of the talo-navicular joint or from tarso-metatarsal dislocation.

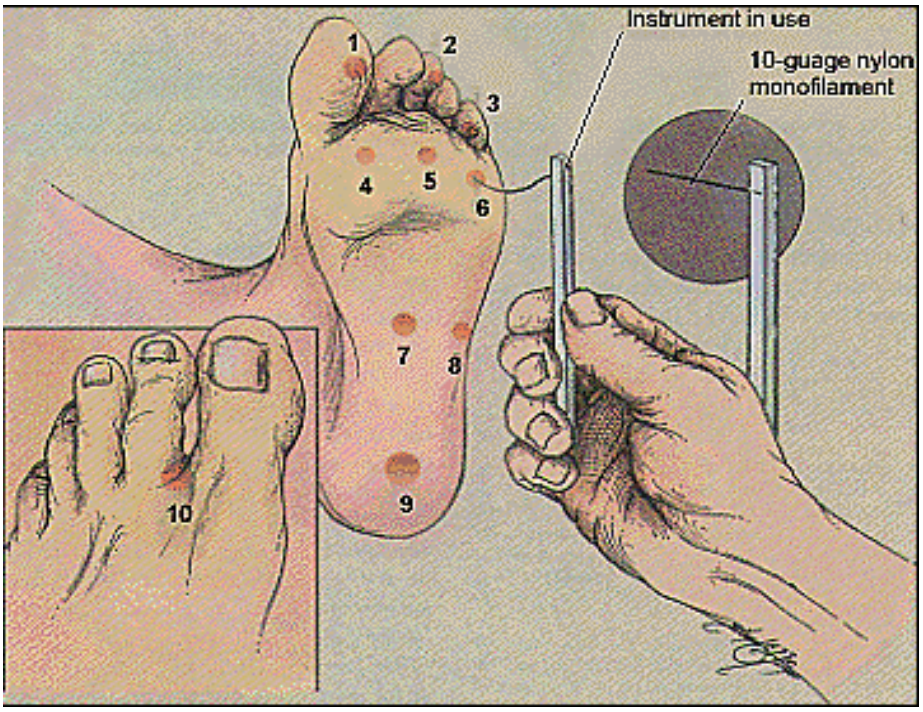
Both are often associated with a bony prominence which is very prone to ulceration. Healing is notoriously difficult. If these deformities are not diagnosed early and accommodated in properly fitting footwear, ulceration at vulnerable pressure points often develops. It is not uncommon to mistake acute charcot foot for cellulitis and osteomyelitis. If the affected foot is elevated, the erythema of charcot foot will recede whereas that of cellulitis will persist. Acute charcot foot should not be mistaken for a cellulitis and operated .

Plain X-ray of the foot will show demineralization, bone destruction and periosteal reaction. Marked osseous resorption of bone results in “pencil pointing” and “sucked candy” deformities of the metatarsal heads and shafts. In the largest joints of the foot there will be destruction of bone and new bone formation. It is a dictum that a “warm swollen foot in a diabetic with neuropathy without local and systemic signs of infection, charcot foot must be considered until proven otherwise”.

Osteomyelitis

Osteomyelitis should be suspected if the ulcer does not heal for more than 6 weeks of appropriate care and off loading, and if there is swollen foot with ulcer, sausage toe, high WBC count or inflammatory markers. Radiographic evaluation is needed if osteomyelitis is suspected. Bone scan findings will be positive within 24 hrs while a plain X-ray will take 10 – 14 days to show any abnormality. There will be soft tissue swelling and periosteal elevation in acute osteomyelitis and Osteopenia, osteolysis, and tapering of bones in chronic osteomyelitis. Any ulcer in which the bone is felt on probing with a sterile metal probe is likely to have osteomyelitis.

MONOFILAMENT TEST



DIABETIC FOOT -CLINICAL ASSESSMENT

Clinical assessment of Neuropathy

1**.Filament test**- Semmes-Weinstein monofilaments is used to detect the diminished sensation of foot.

Semmes-Weinstein monofilaments

The monofilament is a valuable and easy to use tool. The monofilament is a long nylon wire, the tip of which gives a force of 10 grams. It is pressed against the skin to the point of buckling for atleast one second. The points of testing are plantar aspects of 1^{st} , 3^{rd} and 5^{th} digits, the plantar aspect of 1^{st} , 3^{rd} and 5^{th} metatarsal heads, plantar mid foot medially and laterally and the plantar aspect of heel (10 sites totally) . Neuropathy is said to exist when 4 out of these 10 sites show absence of sensation when the wire is pressed against the skin.

2**.Testing for vibration sense in toes and over the Malleoli**

Biothesiometer

This is also called as vibration perception threshold meter. This has a hand held probe whose tip vibrates at 100HZ. The probe is applied to a part of the foot, usually on the big toe. The probe can be made to vibrate at increasing intensity by turning a dial. The voltage supplied to the probe can be adjusted from 0 -50 V. The probe is placed against the skin

BIOTHESIOMETER

and the voltage is increased until the patient perceives the vibration. Mean of three readings is used to determine the vibration perception threshold for each foot. Normal reading is less than or equal to 25 V.

3. **Loss of joint position** is common in diabetic neuropathy. Joint sense of great toe is tested. Severe neuropathy produces small muscle wasting in the foot which leads to **collapse of arches** and deformity of toes. These are precursors for ulcer formation. **Absence of sweating** makes the foot dry and prone for infection and cracks. Prominent long saphenous vein is an index of **autonomic microcirculatory dysfunction**. This is a valuable clinical sign (J D Ward sign) of microcirculatory arterio venous shunting..

Clinical assessment of vascular disease

It starts with inspection of the foot for hue of toes, nicotine staining of fingers, the thinning of skin due to loss of subcutaneous tissue and acral ulcers. Palpation of pulses (dorsalispedis, popliteal and femoral) remains the corner stone of screening for peripheral vascular disease. Absence of distal pulses is a sure sign of significant arterial disease. However presence of palpable pulse does not absolutely exclude vascular disease.

Right ABI

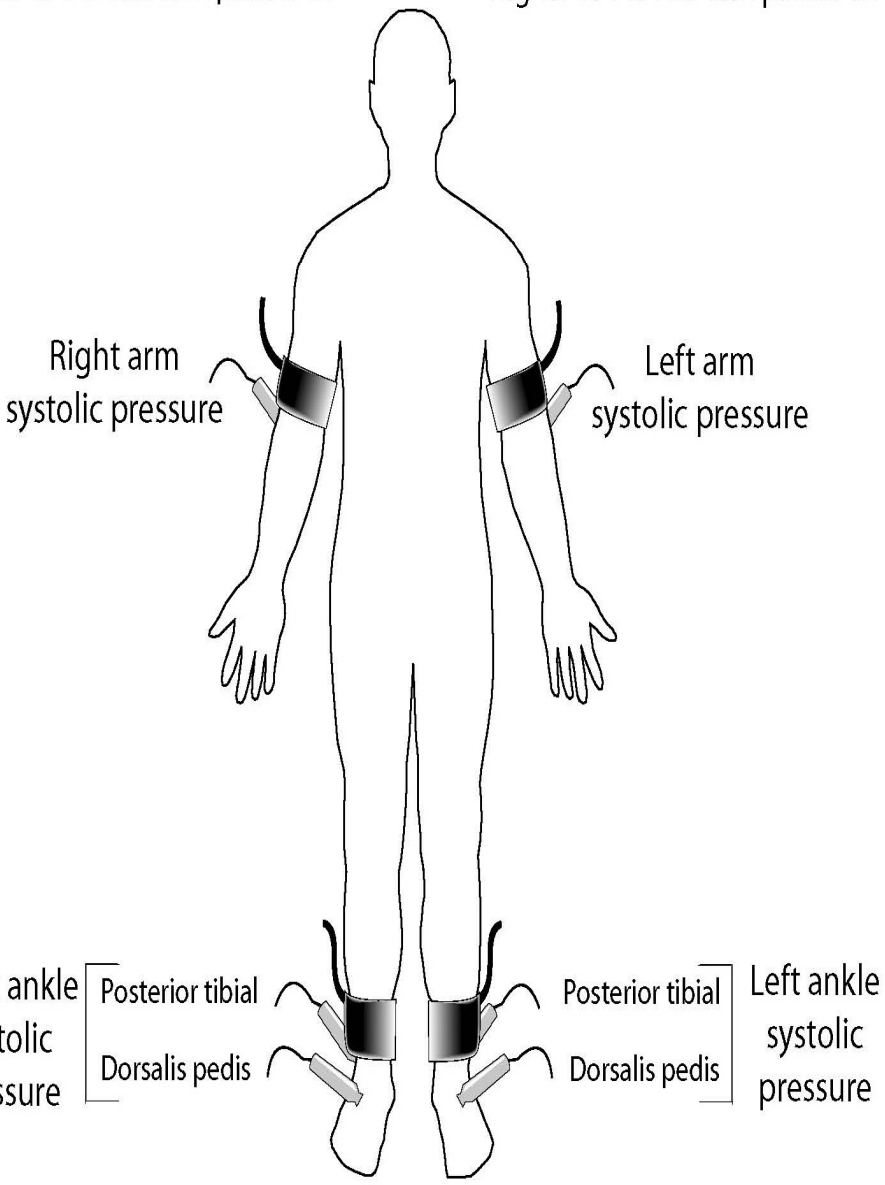
Higher of the two right ankle pressures

Higher of the two arm pressures

Left ABI

Higher of the two left ankle pressures

Higher of the two arm pressures



Ankle brachial pressure index(ABI)

It is a simple method of assessing vascular insufficiency. It is obtained by dividing Ankle systolic pressure by Brachial systolic pressure. Normal values are 1± 0.1. However ABI can be deceptive because calcification of vessels in diabetics can lead to falsely elevated ABI. All diabetics must have an annual assessment of ABI.

Indications for ABI monitoring

1. All those with type 1 diabetes older than 35 years or who have had diabetes for over 20 years at base line.
2. All patients older than 40 years at base line with type 2 diabetes.
3. Any diabetic patient who has newly detected diminished pulses , femoral bruits or a foot ulcer.
4. Any diabetic with a leg pain of unknown etiology.

If ABI is more than 0.9 repeat every 2 -3 years. If ABI is 0.5 -0.89 repeat the measurement within 3 months and treat cardiovascular risk factors. If ABI is less than 0.5, refer for vascular work up and management. If an incompressible artery with an ankle pressure above 300mmHg or an ankle pressure 75 mmHg above arm pressure is found, the measurement should be repeated in 3 months. If still present refer for vascular work up.

Infection

Infected ulcers are often asymptomatic in neuro ischemic foot of diabetics. The categorization of wound infection can be mild, moderate and severe. Mild infections are superficial infections confined to the skin and subcutaneous tissue with minimal or no purulence or cellulitis. Moderate infections are deep and may involve fascia, muscles, tendons, joints and bones. They may present as cellulitis of less than 2cm diameter, plantar abscess and with systemic symptoms. Severe infections are deep with cellulitis more than 2cm,lymphangitis, gangrene and or necrotizing fascitis, threatening limb loss and causing systemic toxicity.

INTEGRATED EXAMINATION OF DIABETIC FOOT

In practice the examination of the foot should be divided into four main parts: inspection, palpation, neurological examination and vascular assessment.

1. Inspection

The foot should be fully inspected including dorsum, sole, back of the heel and inter digital areas with full assessment regarding colour(as an indicator of ischemia), deformity, swelling, callus, skin breakdown, infection, necrosis

2. Palpation

Pulses should be palpated and skin temperature compared between both feet with the back of the examining hand. The measurement of the skin temperature is particularly helpful in the management of the charcot foot where a digital skin thermometer is useful.

3. Neurological examination:

Peripheral neuropathy should be detected either by using the monofilament or biothesiometer or by performing a simple sensory examination.

4. Vascular status:

All the peripheral pulses must be examined and compared with the normal limb. With regard to lower limb, femoral, popliteal, dorsalis pedis and posterior tibial arterial pulses must be examined.

DIABETIC FOOT – INVESTIGATIONS

LABORATORY TESTING :

1. Blood sugar monitoring is the corner stone in management of any diabetic problem. A fasting and postprandial plasma glucose monitoring is essential in all diabetic foot patients. HBA1c monitoring is widely practiced nowadays.

2. Bacterial culture

Superficial swabs are not useful. Necrotic tissue should be removed before taking a swab. Culture of swabs taken from the deeper part of the wounds will be effective in identifying the pathogens.

IMAGING STUDIES :

Plain Radiographs are used to detect osteomyelitis, osteolysis, fractures, dislocation, etc . In a **CT scan,** the resolution of bone with osseous fragmentation and subluxation are well visualized. **MRI** aids in diagnosis of osteomyelitis, deep abscess, septic joint and tendon rupture. **Three phase Technetium Scans** are used for early detection of osteomyelitis, fractures ,charcot arthropathy**. Indium III Leucocyte scans and Tc 99 labelled White Cell Scan** – differentiates osteomyelitis and neuropathic arthropathy. **Duplex ultrasound and Arteriography** are used to detect arterial stenosis.

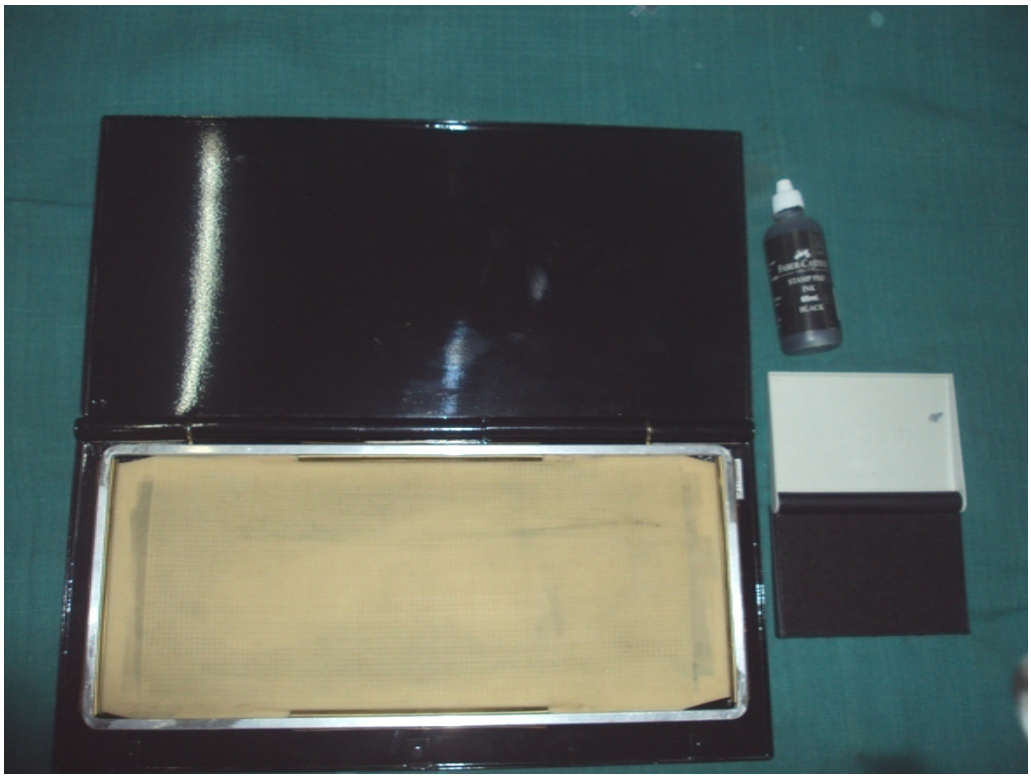
Gait analysis and Thermography

A walking cycle by definition is the time between the heel making contact with the ground and the same heel again coming in to contact with the ground. In diabetes thickening of skin of sole due to abnormal weight bearing and infection under thick skin leads to altered gait. Neuropathy leading to claw toes and bent toes can lead to ulcers. Hence gait analysis in diabetics is mandatory for early detection of neuropathy.

Moderate repetitive stress with repetitive shearing force produces the typical neuropathic ulcer. Frictional forces occurring below the calcaneum is longitudinal while in forefoot it is both longitudinal and transverse. In a normal as well as in insensitive feet, walking briskly is accompanied by progressive hyperemia over points of maximum stress. Thermography helps to outline the temperature contrast of progressive inflammation from such a process. In subjects with insensitive foot thermographic pattern shows hyperemia at sites of old scar, there by inferring that these subjects have been stressing that particular area more than optimally, due to absence of pain and as a result of motor neuropathy. Similarly, in- shoe foot prints help to detect the points of persistent and maximum stress on the feet which probably could be alleviated by proper footwear.

HEALING ULCER

HARRIS FOOT MAT



Harris mat

The feet can be evaluated for high pressure points by means of devices that can quantitate the pressure under the foot during walking or standing. A relatively inexpensive method to establish the presence of pressure points is the harris foot mat. This is an ink pad with graded depths of grid lines. The patient walks across the pad and the pressure points can be assed by the intensity of the ink. This can also be fed in to a computer and a color coded analysis of pressure points can be obtained which is called as **podio scan**

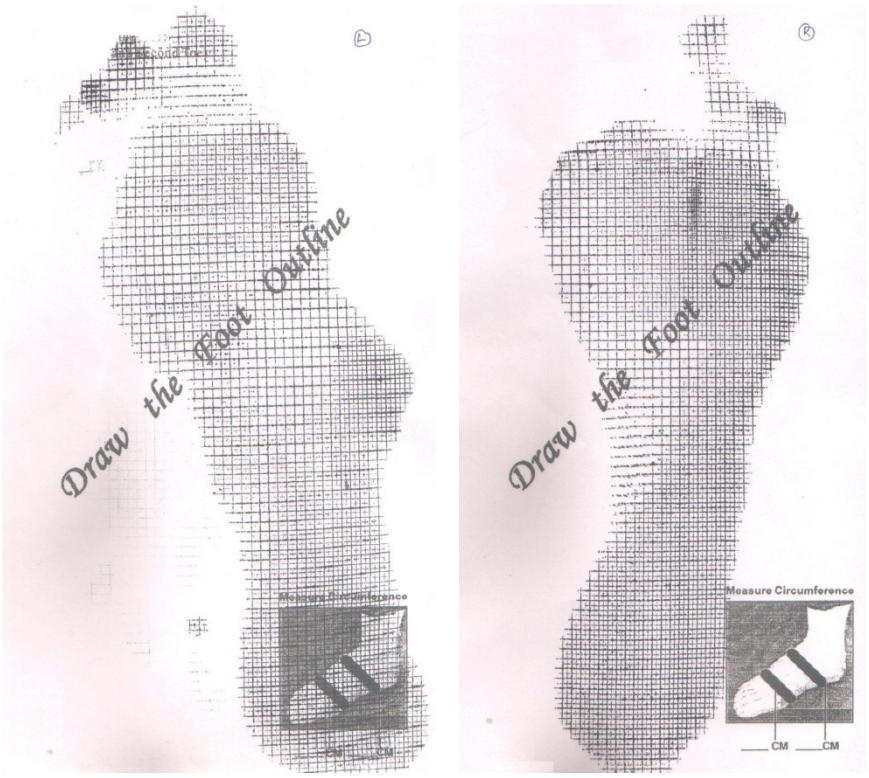
Plantar pressure measurement

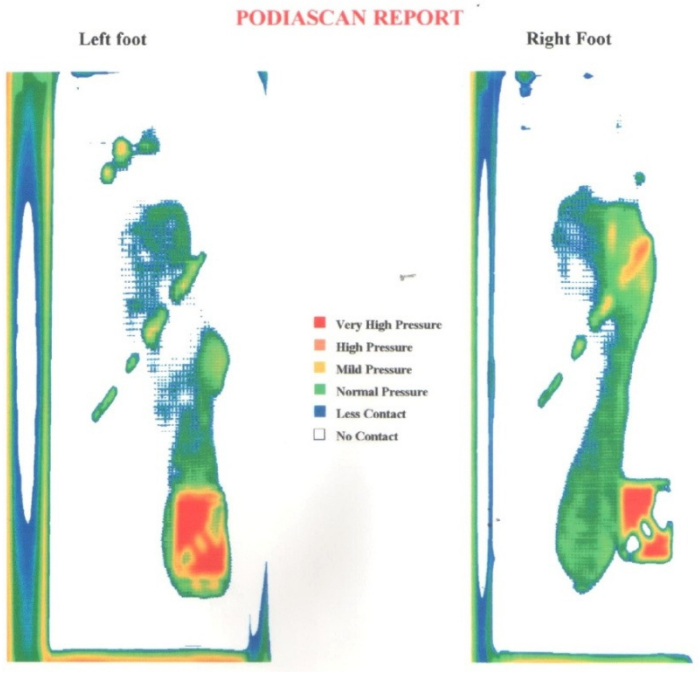
Both the rear foot and fore foot pressures are elevated in diabetics. Restriction of movement of subtalar joint also leads to high plantar pressures. The areas of high pressure ultimately lead to tissue breakdown and ulcer formation. Computerized assessment of foot pressures is very important in assessing the changing pattern of pressure transmission in the feet Plantar peak pressure more than 70N / cm2 is elevated..

Transcutaneous oximetry

It is measured at the dorsum of foot with patient in supine position. A transcutaneous oxygen tension of more than 55mmHg is normal, less than 40mm Hg leads to failure of wound healing and less than 30mm Hg predict limb loss.

FOOT IMPRINT





WAGNER'S ULCER GRADING

Grade – 1

Grade - 2

Grade – 3

Grade - 4

Grade – 5

CLASSIFICATION OF DIABETIC FOOT ULCERS

Wagner classification system

Grade	Lesion
0	No open lesions: may have deformity or cellulitis
1	Superficial ulcer
2	Deep ulcer to tendon or joint capsule
3	Deep ulcer with abscess, osteomyelitis, or joint sepsis
4	Local gangrene- forefoot or heel
5	Gangrene of entire foot

University of Texas classification system

Stage	Grade			
	0	1	2	3
A	Pre or post ulcerative lesions completely epithelized	Superficial wound not involving tendon, capsule, or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	Infected	Infected	Infected	Infected
C	Ischemic	Ischemic	Ischemic	Ischemic
D	Infected and ischemic	Infected and ischemic	Infected and ischemic	Infected and ischemic

MANAGEMENT OF DIABETIC FOOT

The foot ulcers in diabetics are not non healing ulcers but they are maltreated ulcers. Factors leading to wound healing deficiencies in diabetes are decreased or impaired growth factor production, angiogenic response, macrophage function, collagen accumulation, epidermal barrier function, quantity of granulation tissue, keratinocyte and fibroblast migration and proliferation, poor expression of matrix metalloproteinases and their inhibitors

(a) WAGNER grade 0 foot:

This includes patients with apparently normal foot, varying degrees of neuropathy or joint deformities. They may not have any ulcer or infection but are potentially “at risk”. They need regular assessment atleast annually. Neuropathy must be looked for during each assessment. The best way to prevent neuropathy or delay it is to keep blood sugar under control.

Assessment of vascular status is also mandatory. Absent foot pulses even in the absence of claudication or rest pain indicates significant vascular disease and such patients may be suitable candidates for vascular reconstruction or angioplasty. Remember that a diabetic may not manifest claudication symptoms if he had neuropathy.These “at risk” patients may have elevated pressure over some points on the sole. They need appropriate footwear (extra

depth shoes with cushioned insoles). Charcot's feet need custom shoes. Regular trimming of callus is needed. These patients also need advice regarding care of feet..

(b) WAGNER grade 1 foot:

These are patients who have presented with either cellulitis or a superficial ulcer. Ulcer occurs either with repetitive low pressure or sustained high pressure (>6kg/cm) at that point on the sole during walking. Relief of pressure is the mainstay of ulcer treatment. An ulcer will not heal if the patient walks on it. A variety of ways are available to "off load" the ulcer. These include complete bed rest, use of total contact casts, walkers, braces etc. As in the case of grade 0 feet, appropriate management of vascular disease is needed. Infection needs antibiotics and debridement as appropriate. Education, foot care, foot wear and regular careful follow up are the principle factors in management of grade 1 foot.

(c) WAGNER grade 2 and 3 foot:

These are patients with deep ulcer with or without complications like abscesses and osteomyelitis. These patients need aggressive surgical debridement. Osteomyelitis must be appropriately managed by debridement/ excision of infected bone. Once the ulcer has healed, the patient needs long

term care to advise appropriate foot wear and also education regarding foot care, in order to avoid recurrence.

(d) WAGNER grade 4 and 5 foot:

These are patients who have either localized or extensive gangrene. They need minor or major amputation respectively. Almost always there is vascular occlusive disease. These patients therefore need appropriate surgical amputation followed by vascular reconstructions. Aftercare involves special footwear for the ipsilateral and contralateral foot. (These patients tend to over use the other foot and develop ulcers of the opposite foot). In case of major amputees, prosthetic devices need to be fitted in order to mobilize the patient. Mortality rate of diabetes after a major amputation is nearly 50% at one year.

VARIOUS TREATMENT MODALITIES

1. **Protective dressing**

Modern moist dressings include Foams, calcium alginates, hydrogels, hydrocolloids, and adhesive membranes

2. **Topical antiseptics**

Superoxide solutions are useful topical antiseptics which are active against many organisms.

3. **Drainage of pus**

Vaccum assisted drainage (continuous negative pressure of 125 mmHg) to the wound will promote healing of the ulcer.

4. **Debridement**

Aggressive ongoing surgical debridement converts a chronic non healing ulcer in to an acute healing wound. Adequate debridement of necrotic tissue (eschar, slough) is needed before adequate assessment and staging can be accomplished. There are several methods for wound debridement, including sharp surgical, mechanical, enzymatic and autolytic. It is continuum from flushing away debris with low pressure irrigation to wide excision.

Sharp surgical debridement

The most selective and efficacious method of debridement is sharp surgical debridement . Debridement of the hyperkeratotic rim and ulcer base to bleeding is the optimal method of debridement for the patient with an ulcer.

Autolytic debridement

Autolytic debridement with moist interactive dressings (hydrogel , alginates, transparent films, hydrocolloids) is selective and liquefies slough and eschar as well as promotes granulation tissue formation.

Mechanical Debridement

Mechanical debridement may be accomplished with wet to dry gauze dressings , irrigation , pulsatile lavage or whirl pool.

Enzymatic Debridement

Historical enzymes (collagenase, papain, urea) have been used as debriding agents for eschar and slough. They have a selective action, but are slow, costly and labor intensive.

5.Antibiotic

The use of double or triple antibiotics seems to be justified. The antibiotics used must have broader spectrum covering gram positive, gram negative and anaerobic organisms.

MANAGEMENT OF INDOLENT NONHEALING ULCERS

A. **Collagen sheets and powders**
B. **Silver dressing**
C. **Growth factors**

Growth factors are derived from platelets, bioengineered tissues or by recombinant techniques.

PLATELET DERIVED GROWTH FACTOR (PDGF)

Alpha granules from platelets contains numerous growth factors. Platelet derived growth factor was one of the first characterized and has led to an understanding of the mechanism of many growth factors. Platelet-derived growth factor (PDGF) regulates cell growth and division. In particular, it plays a significant role in blood vessel formation (angiogenesis), the growth of blood vessels from already-existing blood vessel tissue. In chemical terms, platelet-derived growth factor is dimeric glycoprotein composed of two A (-AA) or two B (-BB) chains or a combination of the two (-AB).Though it is synthesized, stored and released by platelets upon activation, it is produced by a plethora of cells including smooth muscle cells, activated macrophages, and endothelial cells. There are five different isoforms of platelet derived growth factor that activate cellular response through two different receptors. Known ligands include A (*PDGFA*), B (*PDGFB*), C (*PDGFC*), and D (*PDGFD*), and an AB heterodimer and receptors alpha (*PDGFRA*) and beta (*PDGFRB*)

Mechanisms

Platelet derived growth factor binds to platelet derived growth factor receptors ligand binding pocket located within the second and third immunoglobulin domains. Upon activation by platelet derived growth factor , these receptors dimerise, and are "switched on" by auto-phosphorylation of

PLATELET DERIVED GROWTH FACTOR

HEALED ULCERS

several sites on their cytosolic domains, which serve to mediate binding of cofactors and subsequently activate signal transduction, for example, through the PI3K pathway progenitor cells. Platelet derived growth factor stimulates and recruits macrophages, neutrophils, and fibroblasts;stimulates angiogenesis, stimulates granulation tissue formation, wound contraction and wound remodelling.

Uses

Recombinant human platelet derived growth factors is approved for treatment of chronic non healing wounds. Plermin gel is used in nonischemic clean wounds. It is applied once daily. With appropriate wound care it increase the incidence of complete wound closure and decrease the time to complete wound closure .

In the study by Smiell JM and Wieman et al, a total of 922 patients have been studied in well designed and controlled trials and have resulted in data supporting safety and benefits of platelet derived growth factor application. It states that in diabetic foot ulcers platelet derived growth factor gel application in conjunction with good wound care , significantly increased the incidence of complete wound closure and significantly reduced the time to complete closure of chronic diabetic neuropathic ulcer.

In the study by Gerit D.Mulder, recombinant platelet derived growth factor application once a day for diabetic foot ulcers resulted in rapid granulation which are grafted there by avoiding limb loss. Steed e all, studied the effects of debridement on response to rhPDGF-BB in randomized placebo controlled studies. Debridement in conjunction with growth factor therapy resulted in statistically significant improvement between placebo and drug therapy. In a study by B.Amnian et al, at Shiraz University of Medicine, topical application of platelet derived growth factors in chronic diabetic foot ulcers lead to accelerated epithelisation of wounds.

CONTRA INDICATIONS

The contraindications for platelet derived growth factor usage are malignancy at the site of the ulcer, wounds that show exposed joints, tendons, ligaments, or bone, an unusual or allergic reaction to plermin, parabens, metacresol or other preservatives, pregnant or trying to get pregnant and breast-feeding.

SIDE EFFECTS-

Reddened skin and skin rash near ulcer are some of the side effects of platelet derived growth factor application.

RETROGRADE VENOUS PERFUSION TECHNIQUE

VENOUS CANULATION

TOURNIQUET APPLICATION

D. RETROGRADE VENOUS PERFUSION TECHNIQUE (RVP):

Ferreira first introduced retrograde venous perfusion technique in 1989 for cases of diabetic neuropathic pedal ulcers. Retrograde venous perfusion is a therapeutic concept based on the Bier's principle of retrograde transvenous perfusion of the capillary circulation during artificially discontinued circulation in the extremities, ensuring a high concentration of effective substances in the target tissues.

Mechanism of action

Diabetic and ischemic ulcers are manifestations of breakdown in blood supply as a result of impairment in microcirculation and therefore remain resistant to systemic therapy. Retrograde venous perfusion induces a dilatation of venous capillaries, post capillary venules and lymphatics while arterioles remain unaffected. Loosening of contacts between endothelial cells and pericytes with focal formation of small gaps in the vessel wall enhances the filtration and diffusion of molecules of drugs in the interstitial tissue leading to a high concentration of the administered drugs in the target tissues.

DRUGS

VA SCULAR DOPPLER

Technique of retrograde venous perfusion

The vein in the lower leg was canulated towards the ulcer and the leg was elevated for 10 minutes to empty the veins. A Sphygmomanometer cuff was applied to the lower thigh while the leg was still elevated and inflated to a level higher than systolic pressure of the patient. The agent(s) to be employed was slowly injected into the vein, diluted in 120mL of saline. After 20 min of injection, pressure was released.

Drugs used

Combination of heparin, sodium bicarbonate, antibiotic and lignocaine.

a. Heparin prevents intravascular thrombosis due to venous stasis.
b. Sodium bicarbonate combats local acidosis and makes the injection less painful.
c. Intravascular lignocaine leads to reduction of vascular tone and increases perfusion.
d. Specific antibiotic can be selected on the basis of culture and sensitivity.

Advantages

a. In a study by El Sarky Mel s et al it was proved that, retrograde venous perfusion does not produce cellular damage of blood and lymphatic vessels.

b. In studies by Siedel, Jochmann etall, Brunner M Goring, the drug concentration in retrograde venous perfusion is reported to be 2.5–7 times higher than by systemic intravenous infusion and three times higher than by a direct intra-arterial route.

c. In systemic intravenous therapy the locally diseased arterial tree in the treated limb compromises delivery of the therapeutic agents to the target tissues.

d. Direct intra-arterial injection has the disadvantage of using the diseased arterial tree in treated limbs, particularly in patients with poor collaterals, as well as the risk of intimal damage leading to thrombus and embolus formation due to the injection.

e. In study by Buhler singer S ,Hiller D et al, showed that retrograde venous perfusion improves the cutaneous microcirculation in the diabetic patients, by shifting blood flow to superficial nutritive capillaries.

f. Several basic and dynamic microcirculatory functions such as measurement of laser-doppler flux and cutaneous oxygen tension studied before and after retrograde venous perfusion suggest that it leads to remarkable improvement of the cutaneous microcirculation, suggesting a

better oxygen supply to the tissues after retrograde venous perfusion therapy.

g. By application of contrast medium and with the help of nuclear medicine studies, it has been shown that the injected fluid penetrates in a retrograde direction into the foot in spite of primarily intact valves.
h. Toxicity of the employed drug is reduced in retrograde venous perfusion because it reaches the target tissue in therapeutic concentrations with relatively low doses and early fixation of drug in the target tissue.
i. In study by Langer K, Partsch et al. retrograde venous perfusion reduces the time of therapy, which is associated with diminishing compliance, cumulative increase in cost, loss of working hours, compromised quality of life as well as overcoming critical complications threatening the foot.
j. It helps in the control of acute episodes of infection, healing of ulcers, reversal of pre-gangrenous state and preparation of affected areas for surgical intervention such as skin grafting.

Disadvantages

The most common problem in retrograde venous perfusion therapy is cannulation of the vein in ischaemic limbs, rashes during the course of treatment, mild pain in the limb during the infusion of drugs and inflation of the cuff, which subsided when the cuff was released.

E. Vascular management

The vascular insufficiency in diabetes can be managed by pentoxyphylline, clopidogrel, Lowmolecularweight heparin for hemodilution and defibrogenation, vascular reconstructive surgery or balloon angioplasty

F. OFF LOADING

Off loading is redistribution of the mechanical force from the foot which helps in altering the skin and soft tissue physiology. Pressure is the causal factor for neuropathic foot ulcers. Therefore removal of pressure should facilitate healing of foot ulcers. This removal of pressure of an affected feet or joints can be achieved by off loading. One way of addressing this problem is prescribing therapeutic shoes.The more effective way to offload the fore foot of patients with neuropathic foot is through the use of rocker sole principle. The other offloading modalities are wheel chair, crutches, walker, total contact cast, bi-valved cast, prefabricated walking brace, Unna boot with walking brace, surgical shoe with insert, Pressure relieving ankle foot orthosis (PRAFO) and Charcot's restraint orthotic walker (CROW)

FOOTWEAR RECOMMENDATIONS IN DIABETICS

The recommendations are based on the following grading:

RISK CLASS	FEATURES
0 (low risk)	Has normal protective sensation
1 (medium risk)	Has neuropathy but no deformity or previous ulceration or amputation
2(high risk)	Neuropathy + deformity present But no previous ulceration or amputation
3(very high risk)	Neuropathy + deformity + history of previous ulceration or amputation

Risk class 0:

Essentially normal patients. They need to be adviced to wear shoes with thick sole (to absorb vertical compressive forces) with soft uppers (to mould foot shape and avoid shoe bite) with ample toe box (to be able to wiggle toes).

FOOR WEAR FOR DIABETIC PATIENTS

FOOR WEAR FOR DIABETIC PATIENTS WITH ULCER

Risk class 1:

They are potential candidates for ulcerations, since they have no protective sensation. These patients need advice on foot care (donot walk barefoot, avoid bathroom surgery, avoid extremes of temperature while washing feet), in addition they need foot wear that satisfies all criteria for all class "0" but also has a pressure dissipating accommodative insole(to avoid local high pressures).

Risk class 2:

These are neuropathic patients with foot deformity (such as bunions, claw toe, hammer toe).They need a footwear with extra soft accommodative uppers that mould to the foot's shape while allowing enough shape for toe movement. The sole may need to have recessed heel (to reduce impact at "heel strike" phase of gait) along with angulation of the sole just behind the metatarsal heads (so that a rolling motion is obtained during walking – like a "rocker- bottom"). A total contact insert is beneficial.

Risk class 3:

These are patients who have already ulcerated once and likely to do so repeatedly. They need footwear recommendations as for a grade 2, well fitting shoes with a rocker bottom sole and moulded insole.

In case of patients with active ulceration, various options are available to off- load the foot. These are: total contact cast, air cast or patellar tendon weight bearing brace, temporary shoes(talus shoes, which has no sole in the front that patient walk only on heel), customized foot wear (applicable to patients with charcot's foot who have disrupted bony architecture of foot).

G. Surgical management

This may be curative or ablative

Curative Surgery

The aim of curative surgery is to remove areas of chronically increased peak pressure. The curative operative procedures includes exostectomy, digital arthorplasty, sesemoidectomy, metatarsal head resections, joint resections, partial calcanectomy .

Ablative Surgery:

The aim of ablative surgery includes removal of all infected & necrotic tissue to the level of viable soft tissue and bone. Amputations may be toe disarticulation, fore foot amputation, Syme's amputation , below knee amputation

NOVEL THERAPIES

(a). Hyperbaric oxygen therapy (b) Live human skin equivalents produced by tissue engineering techniques which act by filling the wound with extracellular matrix and inducing the expression of growth factors and cytokines that contribute to wound healing. Graft has both epidermal and lower dermal layers and contain human cells. (c).Electrical stimulation, cold laser and heat.

PREVENTIVE STRATEGIES

The International Diabetes Federation has proclaimed 2005 to be 'The Year of the Diabetic Foot'. One rupee spent on prevention is equivalent to one million rupees saved in terms of limbs and life salvaged. Control of blood glucose levels is paramount in minimizing complications related to diabetes. Team members involved in diabetic foot care include a Podiatrist, Internist, Ophthalmologist , Endocrinologist, Infectious disease specialist , Cardiologist, Nephrologists, Vascular surgeon , Orthopedic surgeon , Nurse and Orthotist.

Recurrent ulceration occurred in 58 % of patients whom resume wearing their own foot wear. Self assessment by SW filament and temperature assessment of the foot has been shown to reduce the incidence of foot ulcers.

The self assessment protocol includes

Findings	Category	Frequency of evaluation
Normal		Yearly
SW filament 5/10	1	6 monthly
SW filament 5/10 or PAD or deformity	2	3 monthly
H/O ulcer or minor amputation	3	Monthly

DO's

- Wash feet daily.
- Inspect feet and toes, especially in between, daily.
- Wear thick, soft socks.
- Cut toe -nails straight across.
- Be measured and fitted each time you buy a new pair of shoes.
- Lose weight.
- Exercise.

DONT's

- Never go barefoot.
- Avoid high heels, sandals and shoes with pointed toes.
- Don't smoke and drink only in moderation.
- Avoid soaking your feet.
- Don't wear anything that is too tight around the legs.
- Never use heating pads or hot water bottles on cold feet.
- Avoid over the counter medications for corns, calluses, or warts.

RESULTS

Group A – Saline group – 25 patients

Group B – PDGF group – 25 patients

Group C – RGVP group – 25 patients

Group D – Intravenous group – 25 patients

A. PROFILE OF CASES STUDIED

Table 1 : Age distribution

Age group	Group A (Saline)		Group B (PDGF)		Group C (RGVP)		Group D (Intravenous)	
	No	%	No	%	No	%	No	%
Upto 40 years	6	24	2	8	3	12	4	16
41 – 50 years	7	28	5	20	6	24	9	36
51-60 years	7	28	9	36	10	40	6	24
Above 60	5	20	9	36	6	24	6	24
Total	25	100	25	100	25	100	25	100
Range	32-80		35-75		40-70		25-70	
Mean	51.1		56.7		53.3		51.2	

Age of the patients included in the study ranged from 25 to 75 years. Mean age of the patients was between 51 to 57 years

cc

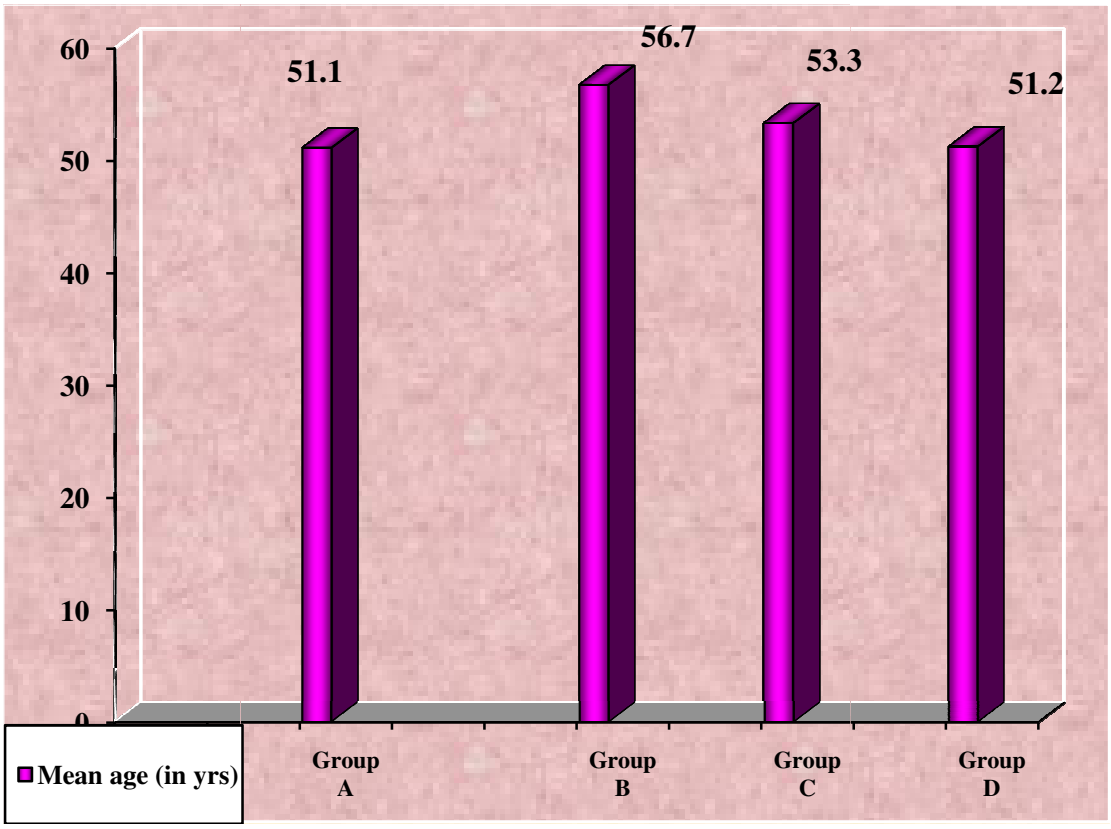


Table 2 : Sex distribution

Sex	Group A (Saline)		Group B (PDGF)		Group C (RGVP)		Group D (Intravenous)	
	No	%	No	%	No	%	No	%
Male	16	64	16	64	19	76	19	76
Female	9	36	9	36	6	24	6	24
Total	25	100	25	100	25	100	25	100

Majority (more than 60%) of cases in all the four groups were males.

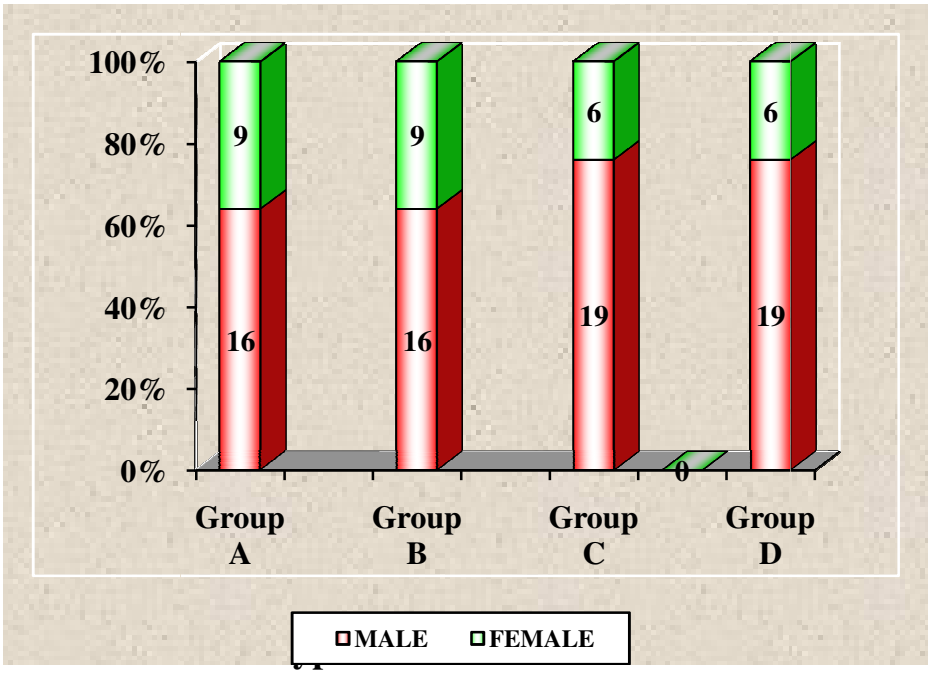


Table 3 Type of diabetes mellitus

Type of DM	Group A (Saline)		Group B (PDGF)		Group C (RGVP)		Group D (Intravenous)	
	No	%	No	%	No	%	No	%
Type 1	-	-	1	4	-	-	1	4
Type 2	25	100	24	96	25	100	24	96
Total	25	100	25	100	25	100	25	100

Except a single case in PDGF and another case in Intravenous Group, all the other 98 cases studied were of Diabetes mellitus type 2.

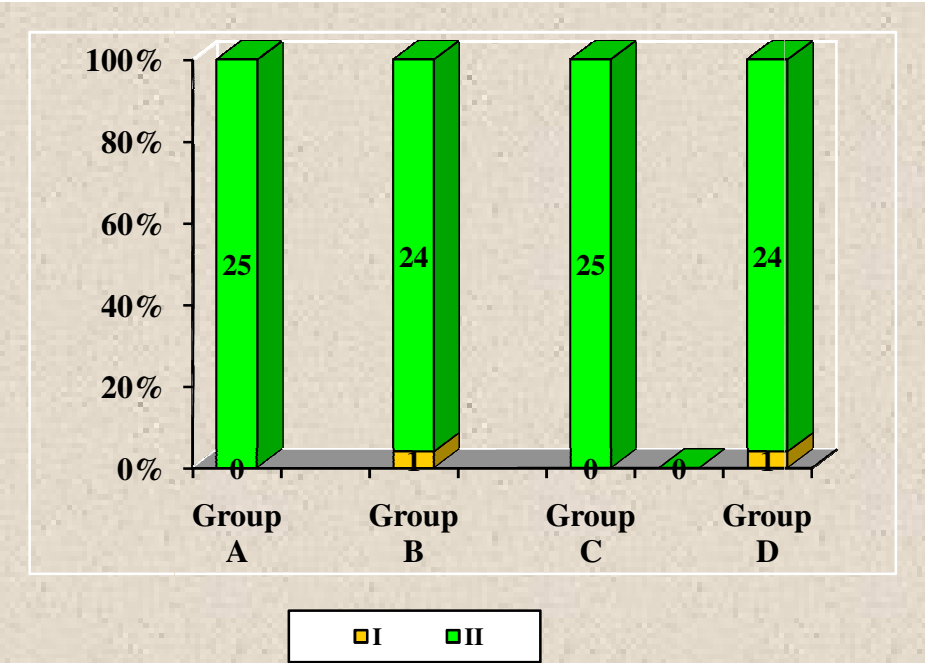
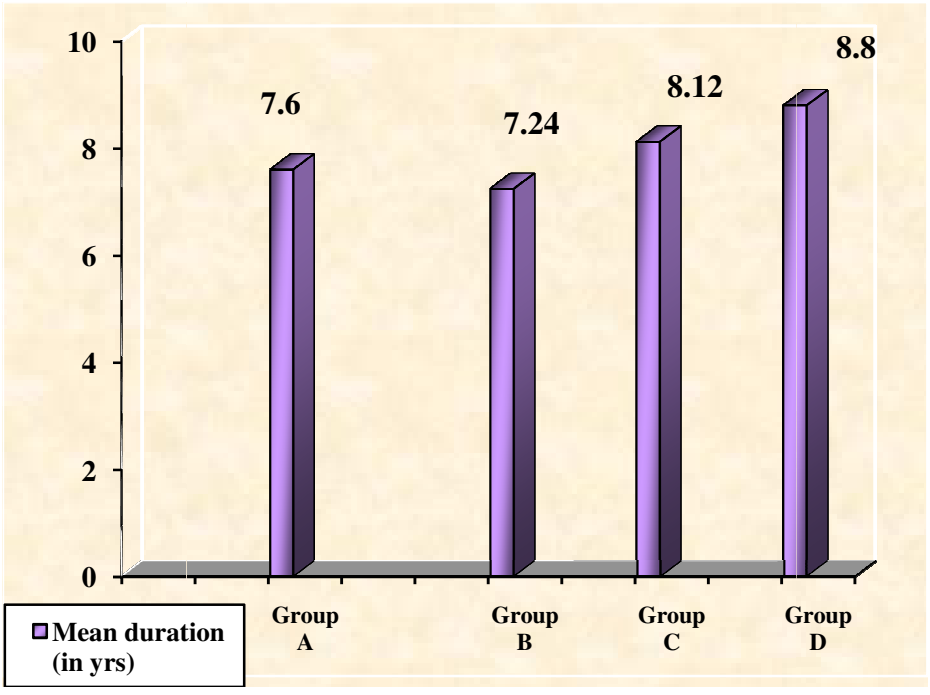


Table 4 : Duration of DM

Duration of DM (in years)	Group A (Saline)	Group B (PDGF)	Group C (RGVP)	Group D (Intravenous)
Range	4-20	3-12	5-12	3-15
Mean	7.6	7.24	8.12	8.8

Mean duration of Diabetes Mellitus in all the diabetic foot ulcer patients was more than 7 years



B : RISK FACTORS

Table 5 : Smoking (Among males)

Smoking (Among males)	Group A(16) (Saline)		Group B(16) (PDGF)		Group C (19) (RGVP)		Group D(19) (Intravenous)	
	No	%	No	%	No	%	No	%
Yes	8	50	9	56.3	5	26.3	7	36.8
No	8	50	7	43.8	14	73.7	12	63.2

Among the males included in the study, percentages of smokers were 50%, 56.3%, 26.3% and 36.8% respectively in the four groups.

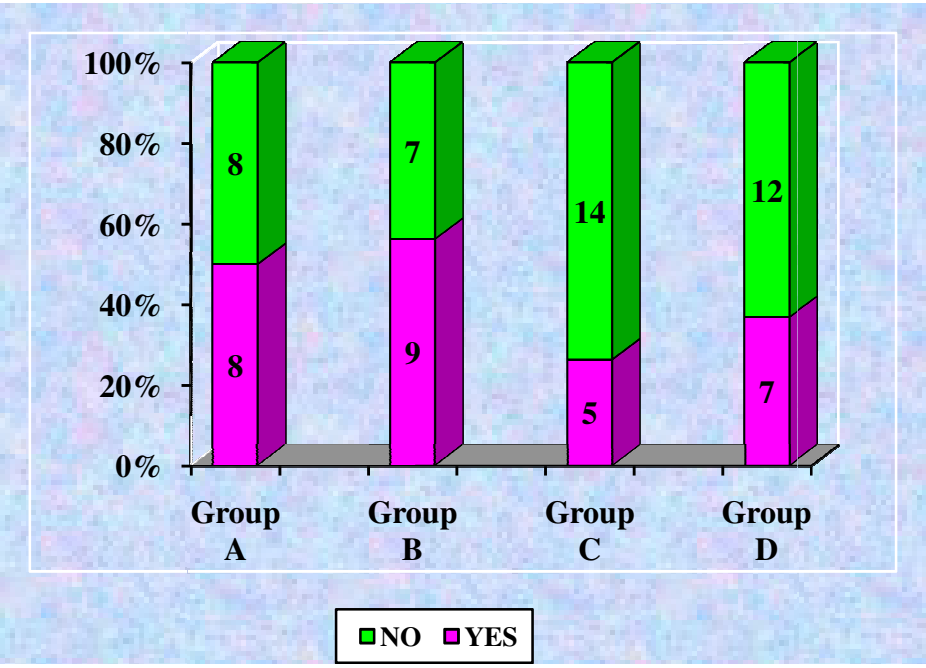


Table 6 : Hypertension

HTN	Group A (Saline)		Group B (PDGF)		Group C (RGVP)		Group D (Intravenous)	
	No	%	No	%	No	%	No	%
Present	16	64	12	48	14	56	12	48
Absent	9	36	13	52	11	44	13	52

Hypertension was present in more than 50% of the patients with diabetic foot ulcers.

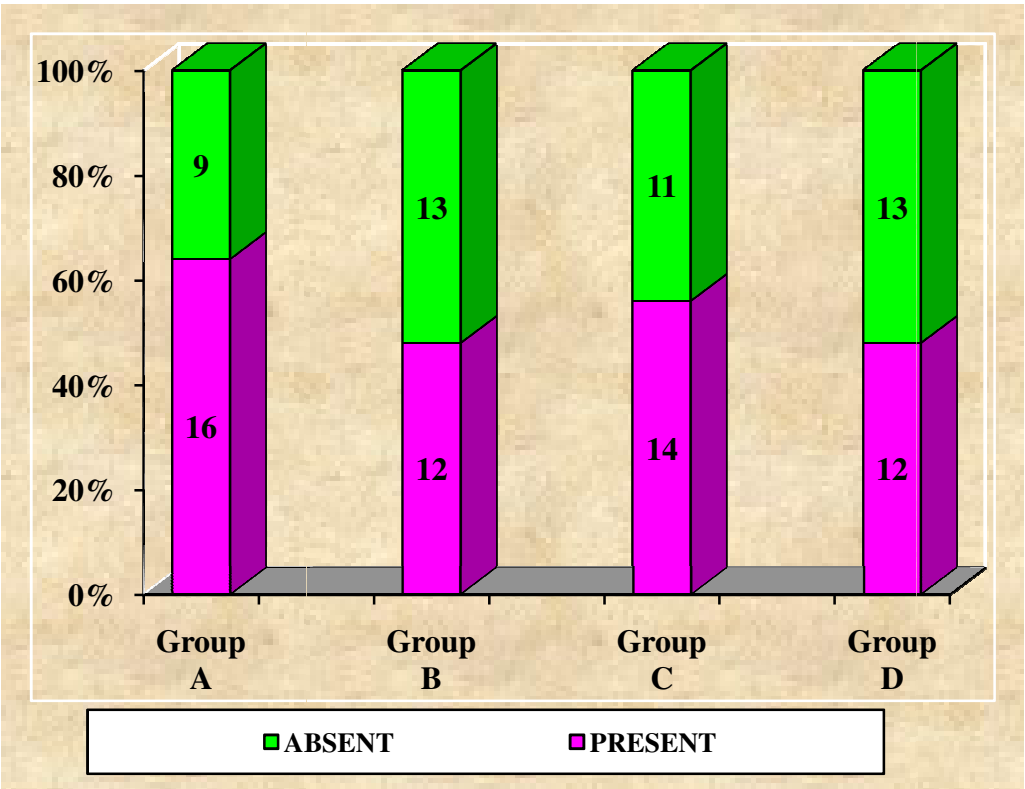


Table 7 : Peripheral Neuropathy

PN	Group A (Saline)		Group B (PDGF)		Group C (RGVP)		Group D (Intravenous)	
	No	%	No	%	No	%	No	%
Present	25	100	25	100	25	100	25	100
Absent	0	0	0	0	0	0	0	0

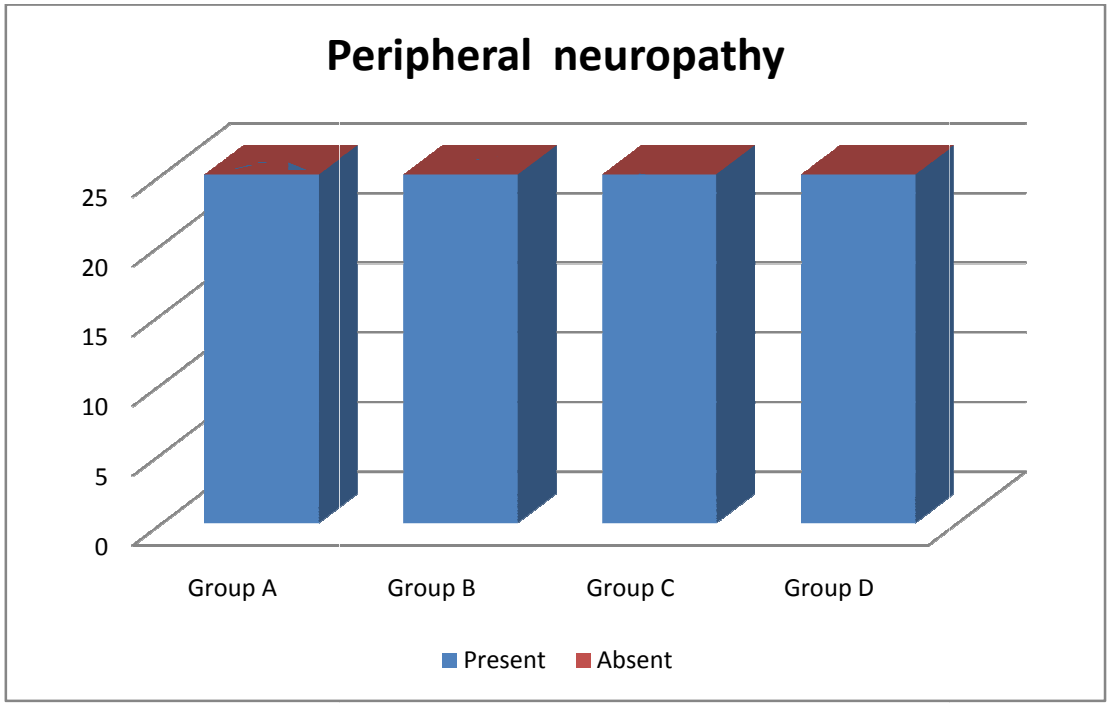


Table 8 : ABI values right

ABI values right	Group A (Saline)	Group B (PDGF)	Group C (RGVP)	Group D (Intravenous)
Range	0.6-1	0.6-1	0.6-1	0.6-1
Mean	0.79	0.73	0.75	0.76
S.D	0.15	0.11	0.13	0.15

Mean ABI – right values were less than the normal value (0.8) in all the 4 Groups.

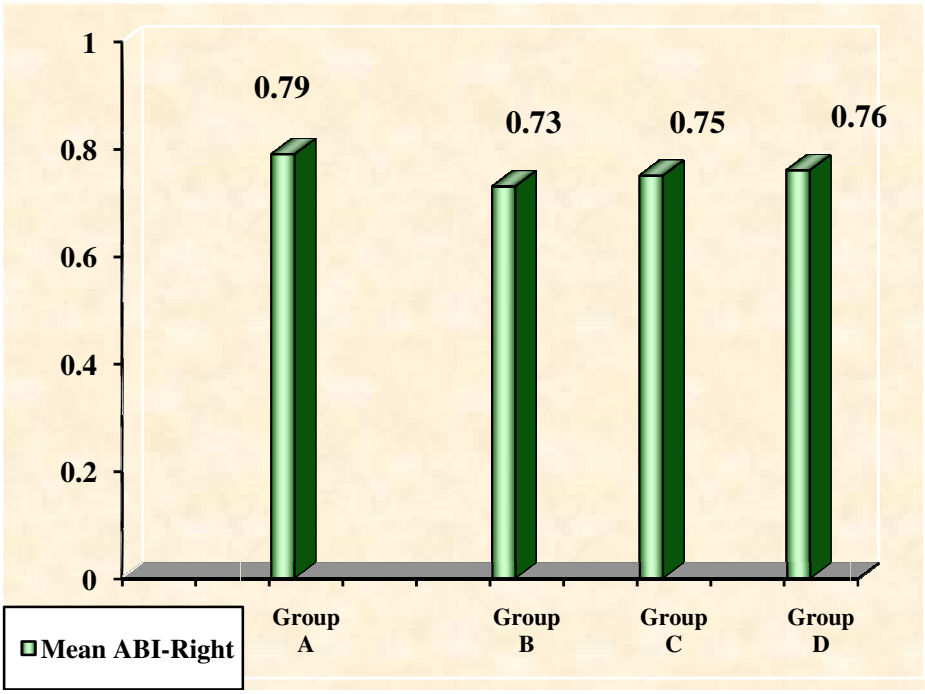
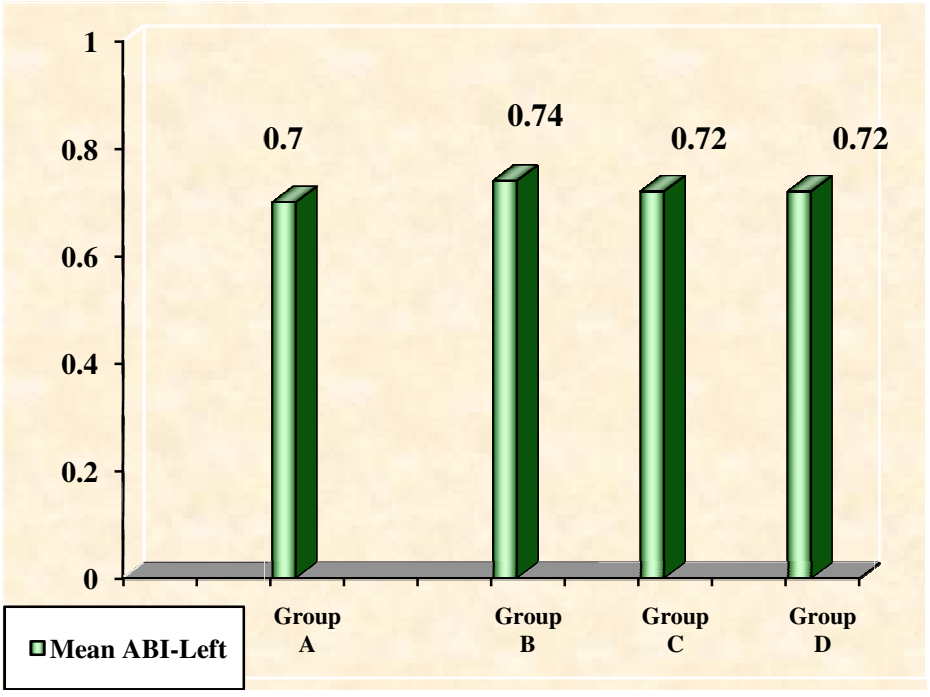


Table 9 : ABI - Left

ABI – Left	Group A (Saline)	Group B (PDGF)	Group C (RGVP)	Group D (Intravenous)
Range	0.6-1.0	0.6-1.0	0.5-1.0	0.6-1.0
Mean	0.7	0.74	0.72	0.72
S.D	0.1	0.13	0.14	0.11

Mean ABI – left values were less than the normal value (0.8) in all the 4 Groups.



C : COMPARATIVE EFFICACY OF SALINE AND PDGF METHODS

Table 10 : Ulcer area at different times

Ulcer area (cm^2) at	**Mean + SD for**		**'p'**
	Saline group	**PDGF group**	
0 day	62.7 ± 28.3	53.2 ± 25.6	0.2297 Not significant
7^{th} day	55.2 ± 27.6	35 ± 20	**0.0088 Significant**
14^{th} day	52.8 ± 27.5	28.7 ± 22	**0.0017 Significant**
21^{st} day	43.9 ± 26.8	22 ± 18.4	**0.0035 Significant**
28^{th} day	41.7 ± 29	21.2 ± 20.9	**0.0063 Significant**
Decrease in 28 days	24.0 ± 18.6	36.9 ± 16.5	**0.0127 Significant**

Ulcer area was 62.7 ± 28.3 $sq.cms^2$ on the day of first visit and it was reduced by 24.0 ± 18.6 to 41.7 ± 29 $sq.cms^2$ at the end of four weeks in the saline group. But the decrease was more (36.9 ± 16.5) in the PDGF group. This difference was statistically significant (p=0.0127).

Ulcer area at different times

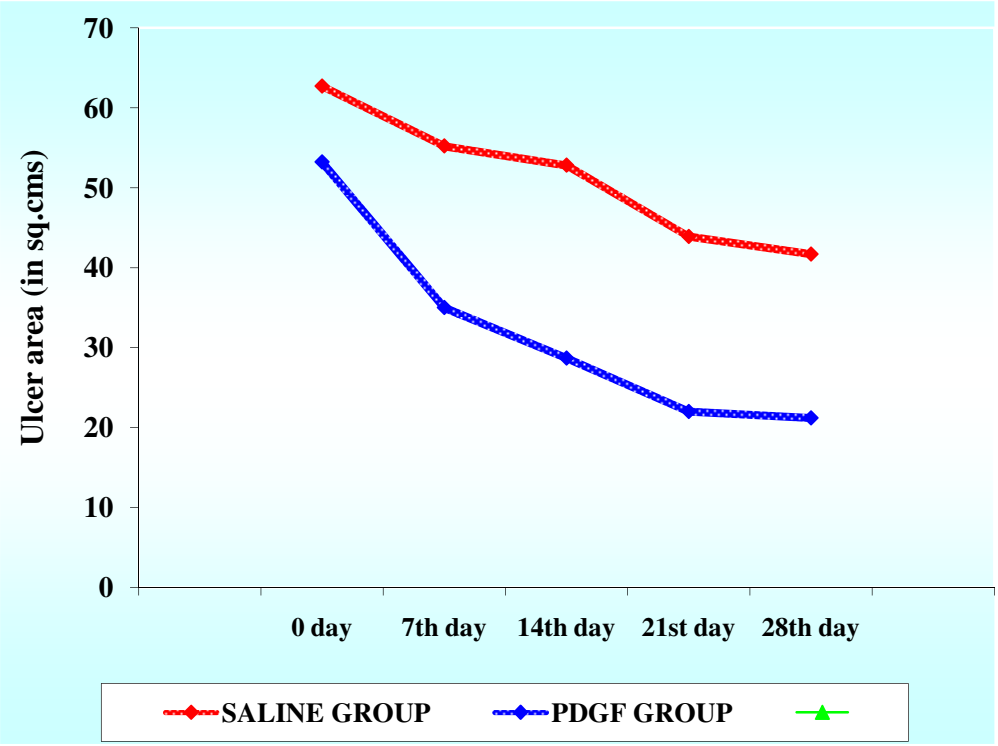


Table 11 : Healing time for completely healed cases

Healing time for completely healed cases (in days)	PDGF group (8 cases)	Saline group
Range	18-20days	24-26
Mean	19	25.0

Two cases in the saline group and 8 cases in the PDGF group were completed healed.

Table 12 : Type of healing

Type of healing	Saline group		PDGF group	
	No	%	No	%
Completely healed	2	8	8	32
Improved	5	20	12	48
Partly healed	15	60	5	20
Worsened	3	12	-	-
P	**0.0007 Significant**			

80% of cases in PDGF group were improved or completely healed whereas this figure was only 28% for saline group. Thus PDGF was significantly (p = 0.0007) more effective in healing than saline group.

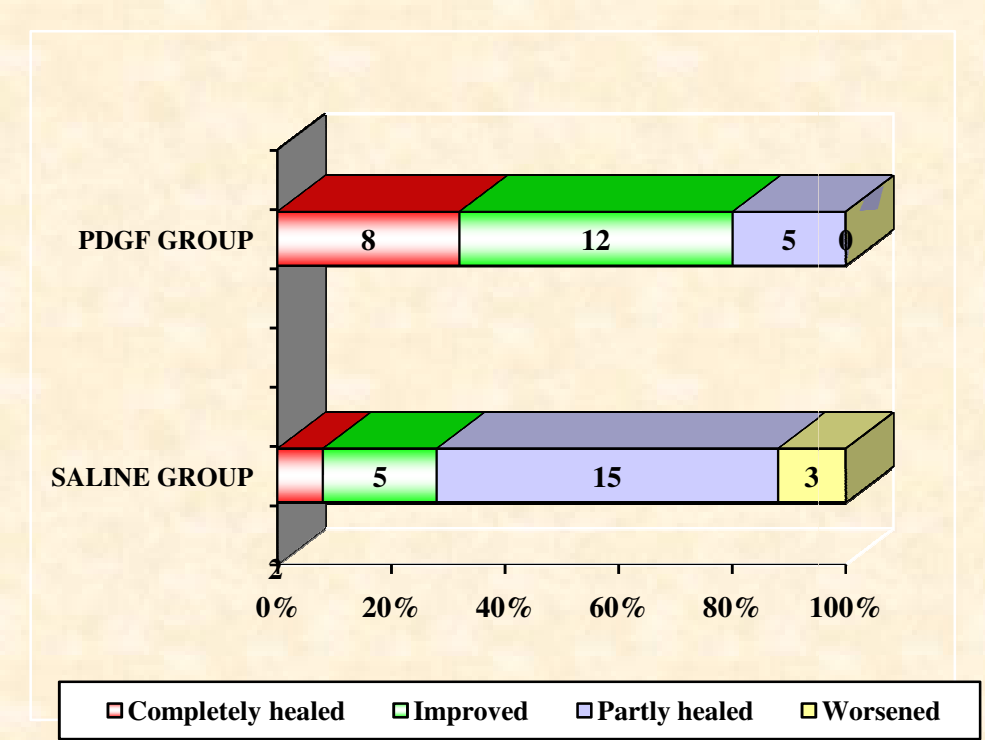


Table 13 : Split Skin Grafting / Amputation

SSG / AMP	Saline group		PDGF group	
	No	**%**	**No**	**%**
SSG				
Done	5	20	8	32
Not done	20	80	17	68
P	0.519 Not significant			
Amputation				
Done	-	-	-	-
Not done	25	100	25	100
p	1.0 Not significant			

SSG was done for 5 cases in saline group and 8 cases in PDGF group. Amputation was not done for any case in both groups.

D : COMPARATIVE EFFICACY OF RGVP AND INTRAVENOUS GROUPS

Table 14 : Ulcer area at different times

Ulcer area (cm^2) at	Mean + SD for		'p'
	RGVP group	Intravenous Group	
0 day	50.9 ±18.8	61.0 ±23.1	0.1785 Not significant
7^{th} day	26.5 ±14.7	46.2 ±19.3	**0.0004 Significant**
14^{th} day	18.9 ±11.1	43 ±23	**0.0001 Significant**
21^{st} day	15.4 ±9.2	35.5 ±22.7	**0.0003 Significant**
28^{th} day	11 ±9.9	31.3 ±19.4	**0.0001 Significant**
Decrease in 28 days	41.9 ±13.9	29.8 ±12.8	**0.0046 Significant**

Ulcer area was 50.9 ±18.8 cms^2 in RGVP group was reduced to11 ±9.9 $sq.cms^2$ at the end of 4 weeks of treatment. But in the intravenous group it was reduced from 61± 23.1 $sq.cms^2$ to 29.8 ±12.8 $sq.cms^2$. The reductions were 41.9 ±13.9 and 29.8 ±12.8 $sq.cms^2$. The difference in reduction of ulcer area was statistically significant (p=0.0046) substantiating the better efficacy at RGVP over intravenous treatment.

Ulcer area at different times

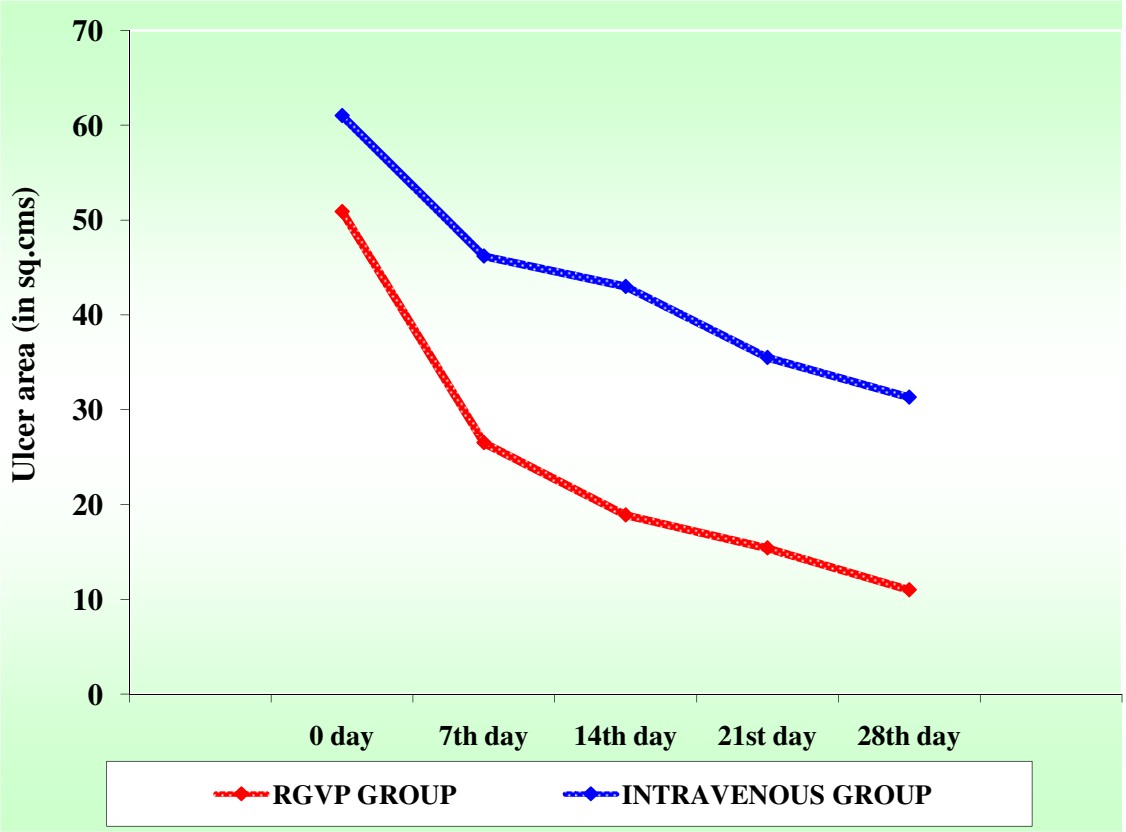


Table 15 : Healing time for completely healed cases

Healing time	RGVP group	Intravenous group
Range	13- 18 days	-
Mean	16 days	-

Note : None of the cases in the intravenous group were completely healed.

Table 16 : Type of healing

Type of healing	RGVP group		Intravenous group	
	No	%	No	%
Completely healed	5	20	-	-
Improved	16	64	6	24
Partly healed	4	16	17	68
Worsened	-	-	2	8
p	**0.0001 Significant**			

84% of cases in RGVP group were improved or completely healed whereas only 24% in intravenous group were improved. Type of healing was significantly better in RGVP group. (p = 0.0001).

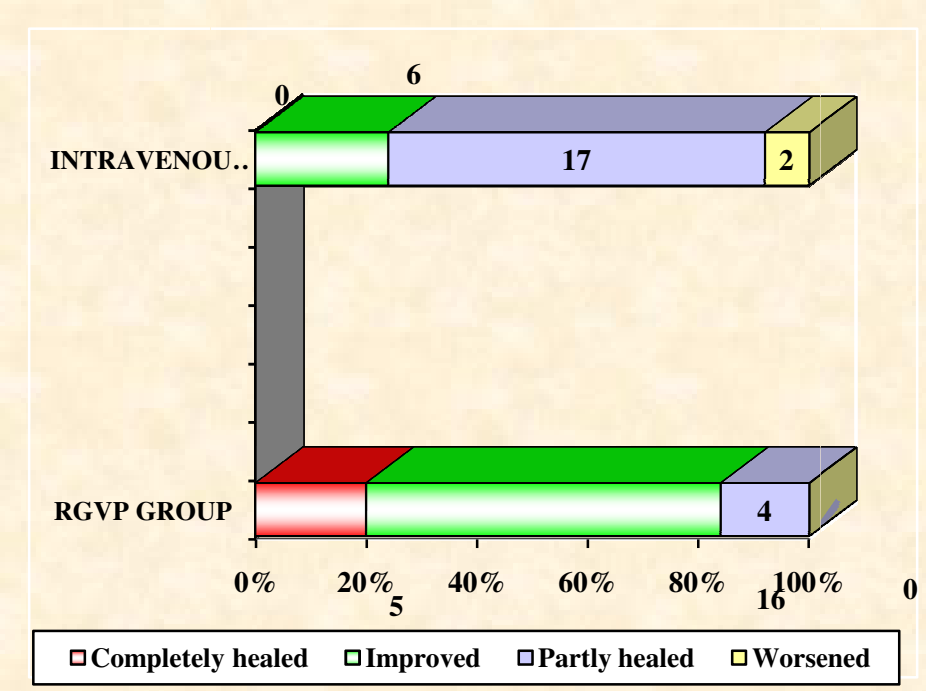


Table 17 : SSG / Amputation

SSG / Amputation	RGVP group		Intravenous group	
	No	%	No	%
SSG				
Done	2	8	3	12
Not done	23	92	22	88
p	0.5 Not significant			
Amputation				
Done	-	-	-	-
Not done	25	100	25	100
p	1.0 Not significant			

Two cases in RGVP group and three in intravenous group were done SSG. None of the cases were amputated.

DISCUSSION AND ANALYSIS

Age and Sex

In our study foot ulcers were more common in male population that too between the age group of 50-60 years. This shows the nature of work in males and the amount of trauma they are subjected to.

Type and Duration of Diabetes

Most of the patients in our study are suffering from type 2 diabetes and the mean duration of diabetes was more than 7 years . This longer duration of diabetes is directly proportional to the development of complications of diabetes like neuropathy and vasculopathy which are significant precursors for foot ulcers .

Risk factors

Smoking as an individual risk factor for diabetic foot ulcer can not be emphasized much. Instead, it accelerates the development of vasculopathy which is a forerunner of foot ulcers. Nearly 50% of the patients in our study had an associated hypertension which in turn accelerates diabetic changes in the tissues at a more rapid pace thereby indirectly leading to foot ulcers.

Neuropathy and vasculopathy

As it is well described in literatures, sensory neuropathy is one of the most important causative factor for development of foot ulcers in diabetics. Our study also confirms the above fact that nearly all our patients had sensory neuropathy. Vasculopathy, a major pathophysiological factor for diabetic foot ulcers was present in about 80% of our patients and in all of them the mean ABI was ≤ 0.8.

PDGF VS SALINE GROUPS

In studies by smiell JM, and wieman et al. and Steed et al., daily application of platelet derived growth factor in diabetic foot ulcers resulted in significant earlier reduction in ulcer area.

In our study also there was a statistically significant reduction in ulcer area of more than $40cm^2$ by 4^{th} week after application of platelet derived growth factor when compared to only $24cm^2$ saline dressing group.

The effective wound healing with application of platelet derived growth factor was proven by the fact that nearly 80% of the ulcers treated with platelet derived growth factor were either improved or got healed completely ,while only 28% of ulcers got improved in the case of saline dressing .

In completely healed wounds the healing time was only 19 days in platelet derived growth factor group when compared to 25 days in saline group.

In patients who were in the improved group the graft bed was better prepared for skin grafting much earlier with dressing platelet derived growth factor than with saline dressing . Hence in larger wounds the platelet derived growth factor dressing provides early and effective wound healing thereby avoiding the need for an extensive skin grafting. Amputations were not done in any of our patients. Platelet derived growth factor dressing is really an useful adjunct and limb salvaging modality in the management of nonhealing diabetic foot ulcers.

RETROGRADE VENOUS PERFUSION VS INTRAVENOUS ANTIBIOTIC GROUPS

The prevalence of infection both the groups were similar as proven by positive cultures from the wound swabs. The effective concentration of antibiotic reaching the ulcer site is much better in the retrograde venous perfusion group compared to intravenous group. This was reflected by the reduction in ulcer area by 28 days was 41cm^2 in the retrograde venous perfusion group compared to only 29 cm^2 in the intravenous group.

Nearly about 80% of the patients in the retrograde venous perfusion group showed a statistically significant reduction in ulcer area compared to only 24% in the intravenous group.

Since effective control of infection is possible with retrograde venous perfusion of antibiotic the ulcer healing occurs much earlier . About 5 patients in retrograde venous perfusion had complete healing of ulcer by 3^{rd} to 4^{tn} week.

Skin grafting was done for 2 patients in retrograde venous perfusion group and none of these patients underwent any sort of amputations. Hence retrograde venous perfusion of antibiotics offers an added advantage of effective drug concentration at the wound site and a better and faster wound healing compared to systemic antibiotic therapy.

PRVENTIVE STRATEGIES

All the patients in our study are screened for the presence high risk pressure points in the same as well as the opposite foot . Special foot wears were prescribed to all our patients to prevent further ulcers in the same or at others sites in their foot. Education regarding foot care was given to all of them and they were advised to come for regular follow up.

CONCLUSION

Diabetes mellitus which is already a public health problem needs to be addressed more effectively. The foot problems in diabetics pose a challenge not only to the treating surgeon but to the entire society. Hence many newer modalities of treatment are being introduced in the management of diabetic foot. There is a changing trend towards adopting limb salvaging procedures thereby avoiding amputations as far as possible.

In our study, foot ulcers were more common in male population, with fairly longer duration of diabetes. This signifies the nature of work that males in our society are exposed to and also the prolonged periods needed for the development of complications of diabetes which are precursors for ulcers in these individuals.

Peripheral neuropathy and vasculopathy are independent risk factors for the development of diabetic ulcers. In our study nearly all the patients had neuropathy and about 80% of our patients had vasculopathy. Hence an adequate control of diabetes by all means is needed to prevent the development of these risk factors in a diabetic individual.

Platelet derived growth factor one of the newer inventions, promotes faster and effective wound healing in diabetic foot ulcers. It’s usefulness in

bringing down the ulcer area is much better than other modalities of treatment. According to our statistical data, about 80% of the ulcers either improved or healed by 4 weeks time which also goes in favour of these statements regarding platelet derived growth factor.

Infection one of the bad prognostic indicator of diabetic ulcer healing needs to be treated more effectively. Retrograde venous perfusion of antibiotics shows more promising results in that it delivered an effective concentration of antibiotics at the wound site thereby promoting ulcer healing in much better and faster rate. Hence these platelet derived growth factor dressing and retrograde venous perfusion of antibiotics are better limb salvaging techniques which can be employed in day to day practice

All the patients in our study are screened for the presence high risk pressure points in the same as well as the opposite foot . Special foot wears were prescribed to all our patients to prevent further ulcers in their foot. Education regarding foot care which is utmost important in diabetic foot management is given to all of them .

By adequate control of blood sugar, proper foot care ,and judicious use of modalities like platelet derived growth factor application and retrograde venous perfusion of antibiotics most of the diabetic limbs can be saved .

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PROFOMA

Name :

Age :

Sex : Male / Female

Ip / Op No. :

DOA :

DOD :

Type of DM : Type 1 / Type 2

Duration of DM :

Comorbidities and Risk factors : Smoking / HTN/ IHD

Treatment : OHA / Insulin/ Insulin +OHA / Antiplatelets

Peripheral Sensory Neuropathy : Present /Absent

Vasculopathy (ABI) :

Right Left

Infection : Present / Absent

Ulcer area(cm2) Day o Day 7 Day 14 Day 21 Day 28

Ulcer healing : RGVP group Intravenous group time(Days)

Ulcer healing : PDGF group Saline dressing group time(Days)

Type of healing : **A / B / C / D**

SSG : Done / Not done

Amputation : Done / Not done

MASTER CHART

SL.NO	Group	NAME	AGE	SEX	IP.NO	TYPE OF DM	DURATION(years)	RISK FACTORS		TREATMENT	PERIPHERALNEUROPATHY	ABI		INFECTION	ULCER AREA (DAYS)Sq.cm					HEALING TIME(DAYS)	TYPE OF HEALING	SKIN GRAFTING	AMPUTATION
								SMOKING	Hypertension			RIGHT	LEFT		0	7	14	21	28				
1	A	Sivakumar	40	1	41655	2	5	P	P	Insulin	+	1	0.7	A	100	90	90	80	80		C	ND	ND
2	A	kuppusamy	66	1	65324	2	6	A	P	Insulin	+	0.7	0.6	A	80	80	70	70	50		C	ND	ND
3	A	Meenakshi sundaram	34	1	70237	2	5	P	A	Insulin	+	0.8	0.7	A	90	80	80	60	60		C	ND	ND
4	A	Alagar	35	1	75072	2	6	P	P	Insulin	+	0.7	0.8	A	80	70	60	45	15		B	D	ND
5	A	Paulraj	65	1	76718	2	10	A	P	Insulin	+	0.7	0.6	A	100	100	90	90	100		D	ND	ND
6	A	Bose	56	1	81238	2	8	P	P	Insulin	+	1	0.8	A	60	50	60	30	10		B	D	ND

7	A	Subbiah	80	1	84619	2	20	A	P	Insulin	+	0.7	1	A	50	45	45	25	10		B	D	ND
8	A	Renga	42	1	86236	2	5	P	P	Insulin	+	0.8	0.6	A	24	20	20	15	15		C	ND	ND
9	A	Narkarunai	52	1	89151	2	4	P	P	Insulin	+	0.7	0.6	A	60	60	40	30	10		B	D	ND
10	A	vijayaraj	32	1	89252	2	4	A	A	Insulin	+	1	0.8	A	36	26	26	24	24		C	ND	ND
11	A	sengol	50	1	531353	2	5	A	A	Insulin	+	0.6	0.7	A	120	100	100	80	80		C	ND	ND
12	A	sivan	50	1	53145	2	8	A	P	Insulin	+	1	0.6	A	40	40	30	10	5		B	D	ND
13	A	ganesh	54	1	18721	2	8	A	P	Insulin	+	0.7	0.6	A	40	30	30	25	25		C	ND	ND
14	A	chandrasekaran	51	1	88351	2	7	P	A	Insulin	+	1	0.7	A	64	56	56	48	40		C	ND	ND
15	A	ilayaraja	39	1	38078	2	4	P	A	Insulin	+	0.6	0.7	A	24	20	20	20	15		C	ND	ND
16	A	sudhakar	45	1	15791	2	8	A	A	Insulin	+	0.9	0.8	A	90	80	70	70	55		C	ND	ND

17	A	irulayee	58	2	75188	2	10	A	P	Insulin	+	1	0.6	A	80	70	60	50	50		C	ND	ND
18	A	ponnalagu	40	2	76496	2	5	A	A	Insulin	+	0.7	0.7	A	80	80	90	90	90		D	ND	ND
19	A	malayalam	60	2	78479	2	12	A	P	Insulin	+	1	0.6	A	50	50	60	60	65		D	ND	ND
20	A	deraviam	63	2	79688	2	12	A	P	Insulin	+	0.8	0.7	A	100	90	90	70	70		C	ND	ND
21	A	muthulakshmi	45	2	83173	2	10	A	A	Insulin	+	0.7	0.8	A	20	10	10	5	-	22	A	ND	ND
22	A	pappathi	55	2	86382	2	5	A	P	Insulin	+	0.6	0.8	A	36	24	12	4	-	24	A	ND	ND
23	A	shenbagam	45	2	89209	2	5	A	A	Insulin	+	0.7	0.7	A	60	50	50	40	40		C	ND	ND
24	A	Pappa	70	2	89468	2	10	A	P	Insulin	+	0.6	0.8	A	24	20	20	20	15		C	ND	ND
25	A	mangayar thilagam	50	2	90769	2	8	A	P	Insulin	+	0.8	0.6	A	60	40	40	36	36		C	ND	ND
26	B	Kumar	44	1	892941	2	5	P	P	Insulin	+	0.6	0.9	A	24	16	16	10	5		B	D	ND

27	B	lakshmanan	75	1	92172	2	12	A	P	Insulin	+	0.7	0.7	A	24	16	8	-	-	20	A	ND	ND
28	B	nagappan	65	1	92235	2	7	P	P	Insulin	+	0.7	1	A	36	24	12	10	5		B	D	ND
29	B	sivalingam	61	1	4863	2	8	A	A	Insulin	+	0.8	0.8	A	50	25	25	10	5		B	ND	ND
30	B	samyvel	60	1	23516	2	7	P	A	Insulin	+	0.7	0.6	A	30	20	10	5		24	A	ND	ND
31	B	ayyappan	60	1	31068	2	6	A	A	Insulin	+	0.6	0.7	A	100	70	60	40	15		B	ND	ND
32	B	marimuthu	35	1	31746	2	3	P	A	Insulin	+	0.8	0.6	A	28	20	8	-	-	18	A	ND	ND
33	B	pondi	50	1	38346	2	6	P	A	Insulin	+	0.7	0.7	A	80	60	40	20	10		B	ND	ND
34	B	michel raj	57	1	44850	2	6	A	P	Insulin	+	0.6	0.7	A	40	30	12	4	-	26	A	ND	ND
35	B	karrupiah	60	1	40540	2	7	A	A	Insulin	+	1	0.6	A	50	25	25	15	10		B	ND	ND
36	B	ramachandran	62	1	88351	2	8	P	P	Insulin	+	0.7	0.8	A	80	60	60	50	55		C	ND	ND

37	B	mahesvaran	41	1	39403	2	10	A	A	Insulin	+	0.6	0.6	A	24	12	8	-	-		A	ND	ND
38	B	sangilimuthu	35	1	21541	1	6	P	A	Insulin	+	0.8	0.7	A	80	60	60	50	50		C	ND	ND
39	B	gurusamy	55	1	398142	2	10	P	A	Insulin	+	0.8	1	A	50	40	15	10	10		B	D	ND
40	B	veerananan	70	1	38925	2	12	P	P	Insulin	+	0.7	0.6	A	36	24	12	8	-	27	A	ND	ND
41	B	sikander	45	1	81256	2	4	A	P	Insulin	+	0.7	0.9	A	100	70	70	60	60		C	ND	ND
42	B	lakshmiammal	55	2	90276	2	10	A	P	Insulin	+	0.6	0.7	A	50	25	15	10	5		B	D	ND
43	B	indhumathi	54	2	93541	2	5	A	A	Insulin	+	0.8	0.8	A	60	30	30	15	10		B	D	ND
44	B	chinnammal	65	2	30701	2	7	A	P	Insulin	+	0.8	0.8	A	40	20	10	5	-	26	A	ND	ND
45	B	pethiammal	45	2	77539	2	7	A	A	Insulin	+	0.7	0.6	A	18	12	6	-	-	18	A	ND	ND
46	B	vijayaraj	60	2	9538	2	8	A	P	Insulin	+	0.7	1	A	50	25	25	15	10		B	D	ND

47	B	lakshmiammal	70	2	7618	2	8	A	A	Insulin	+	0.7	0.7	A	40	20	20	10	5		B	D	ND
48	B	jothi	55	2	25288	2	7	A	P	Insulin	+	1	0.6	A	80	60	60	45	45		C	ND	ND
49	B	pandiammal	74	2	30092	2	5	A	P	Insulin	+	0.8	0.8	A	60	40	40	20	10		B	D	ND
50	B	vairathai	65	2	33094	2	7	A	A	Insulin	+	0.7	0.7	A	100	70	70	50	50		C	ND	ND
51	C	Mani	61	1	51384	2	8	A	A	Insulin	+	1	0.8	A	70	40	20	10	5		B	ND	ND
52	C	sankar	45	1	85601	2	8	P	P	Insulin	+	0.6	0.6	A	50	30	25	25	20		C	ND	ND
53	C	duraipandi	62	1	52681	2	7	P	A	Insulin	+	0.7	0.7	A	60	20	20	10	5		B	ND	ND
54	C	arumugam	53	1	62621	2	12	P	P	Insulin	+	0.6	0.8	A	50	25	25	10	5		B	ND	ND
55	C	pondiaraj	64	1	56021	2	10	A	A	Insulin	+	0.8	1	A	80	60	40	20	10		B	ND	ND
56	C	raju	45	1	66607	2	7	A	A	Insulin	+	0.6	0.8	A	60	40	15	10	10		B	ND	ND

57	C	mahalingam	55	1	45231	2	7	A	P	Insulin	+	0.8	0.6	A	40	24	12	10	5		B	ND	ND
58	C	ramachandran	62	1	88531	2	8	A	A	Insulin	+	0.7	0.7	A	50	20	20	10	5		B	ND	ND
59	C	mohan	40	1	78991	2	7	A	A	Insulin	+	0.6	0.6	A	24	12	4			16	A	ND	ND
60	C	sivamurugan	56	1	52681	2	8	A	P	Insulin	+	0.7	0.7	A	60	40	15	10	10		B	ND	ND
61	C	pandi	55	1	32186	2	6	A	A	Insulin	+	0.7	0.6	A	70	40	20	20	10		B	ND	ND
62	C	kaleswaran	52	1	38126	2	5	A	P	Insulin	+	0.9	0.5	A	44	10	10	10	5		B	ND	ND
63	C	balan	46	1	52621	2	10	P	P	Insulin	+	0.8	0.8	A	90	60	45	40	40		C	ND	ND
64	C	sankar	70	1	14108	2	7	A	P	Insulin	+	0.7	0.5	A	70	30	30	15	10		B	D	ND
65	C	ramani	40	1	28102	2	7	A	P	Insulin	+	0.7	0.8	A	50	20	15	10	5		B	D	ND
66	C	subramaniam	54	1	2418361	2	10	A	P	Insulin	+	0.6	0.6	A	24	10	4			18	A	ND	ND

67	C	kanagaraj	52	1	65212	2	7	A	P	Insulin	+	0.8	0.8	A	30	15	5			17	A	ND	ND
68	C	cheelaiah	60	1	90164	2	7	A	P	Insulin	+	0.8	0.6	A	16	4				13	A	ND	ND
69	C	karuppasamy	52	1	98947	2	12	P	P	Insulin	+	0.7	0.9	A	64	32	32	30	25		C	ND	ND
70	C	mariyammal	65	2	28798	2	12	A	A	Insulin	+	0.6	0.8	A	42	16	12	10	5		B	ND	ND
71	C	kaliammal	50	2	39814	2	10	A	A	Insulin	+	1	0.6	A	40	20	10	10	5		B	ND	ND
72	C	pappa	60	2	74576	2	8	A	P	Insulin	+	0.9	0.7	A	70	40	35	30	30		C	ND	ND
73	C	subbammal	43	2	89650	2	7	A	A	Insulin	+	1	0.6	A	48	18	18	12	5		B	ND	ND
74	C	meenakshi	50	2	360963	2	6	A	A	Insulin	+	0.7	1	A	24	12	10			16	A	ND	ND
75	C	maheswari	40	2	32226	2	7	A	P	Insulin	+	0.8	0.9	A	46	24	12	5	5		B	ND	ND
76	D	Edison paul	70	1	56616	2	10	P	P	Insulin	+	0.7	0.7	A	80	70	70	50	50		C	ND	ND

77	D	ramaiah	55	1	56213	2	10	A	A	Insulin	+	0.6	1	A	60	40	40	20	25		C	ND	ND
78	D	sermakani	64	1	45751	2	12	A	P	Insulin	+	1	0.6	A	42	28	28	20	20		C	ND	ND
79	D	thajudeen	29	1	24699	2	3	P	P	Insulin	+	0.7	0.8	A	28	20	20	18	18		C	ND	ND
80	D	vijayaraj	45	1	43723	2	6	A	P	Insulin	+	0.6	0.6	A	100	70	70	60	60		C	ND	ND
81	D	marriappan	50	1	28410	2	8	P	A	Insulin	+	1	0.7	A	40	20	20	10	5		B	ND	ND
82	D	baskaran	32	1	43126	2	5	P	P	Insulin	+	0.6	0.8	A	28	20	20	16	16		C	ND	ND
83	D	gandhi	49	1	31181	2	8	A	P	Insulin	+	0.7	0.7	A	42	28	28	20	20		C	ND	ND
84	D	raja	67	1	67037	2	8	A	A	Insulin	+	0.6	0.8	A	40	30	25	25	20		C	ND	ND
85	D	mayan	69	1	249024	2	10	A	A	Insulin	+	0.8	0.6	A	30	24	12	10	5		B	ND	ND
86	D	nagaraj	45	1	53921	2	12	A	P	Insulin	+	1	0.9	A	50	40	15	15	10		B	ND	ND

87	D	manoharan	60	1	33851	2	8	A	A	Insulin	+	0.7	0.6	A	80	60	45	40	40		C	ND	ND
88	D	muthu	25	1	34621	1	10	P	P	Insulin	+	0.8	0.7	A	80	80	70	60	50		C	ND	ND
89	D	sankaran	70	1	66513	2	12	A	P	Insulin	+	0.6	0.6	A	48	48	50	54	54		D	ND	ND
90	D	veerapandi	43	1	56365	2	8	P	A	Insulin	+	1	0.7	A	50	40	15	10	10		B	D	ND
91	D	muthupandi	42	1	69546	2	8	P	A	Insulin	+	0.7	0.6	A	100	70	70	60	50		C	ND	ND
92	D	jeyaraman	52	1	98947	2	6	A	A	Insulin	+	0.8	0.7	A	80	60	60	55	55		C	ND	ND
93	D	nachiappan	55	1	78650	2	7	A	A	Insulin	+	0.7	0.8	A	80	60	60	50	50		C	ND	ND
94	D	mohideen	60	1	74210	2	7	A	A	Insulin	+	0.7	0.7	A	48	36	36	24	24		C	ND	ND
95	D	panchammal	68	2	36814	2	10	A	P	Insulin	+	0.9	0.6	A	100	80	100	100	60		D	ND	ND
96	D	chandra	53	2	48189	2	10	A	P	Insulin	+	0.6	0.7	A	80	60	60	50	50		C	ND	ND

97	D	guruvammal	48	2	78290	2	8	A	A	Insulin	+	0.8	0.6	A	40	40	30	20	15		B	D	ND
98	D	anandhi	36	2	98176	2	7	A	A	Insulin	+	1	0.8	A	60	30	30	25	10		C	D	ND
99	D	alagammal	46	2	42986	2	15	A	P	Insulin	+	0.8	0.8	A	60	40	40	20	15		B	ND	ND
100	D	sudha	46	2	64641	2	12	A	A	Insulin	+	0.6	0.8	A	80	60	60	55	50		C	ND	ND